Petition for the Authorization of a Qualified Health Claim for Unsaturated Fatty Acids from Canola Oil and Reduced Risk of Coronary Heart Disease

I. INTRODUCTION

The undersigned, the U.S. Canola Association, submits this petition for a qualified health claim (QHC) in reference to the ability of unsaturated fatty acids (UFAs) from canola oil to reduce the risk of coronary heart disease (CHD) in accordance with the guidance document posted by the Food and Drug Administration (FDA) on July 10, 2003[1]. As FDA requested in that document, this petition addresses all of the elements set forth in 21 C.F.R. § 101.70 for unqualified health claims. The proposed claim would apply to canola oil and certain canola oil-containing products that contain a minimum of 4.75 grams of canola oil (containing approximately 4.4 g UFAs) per reference amount customarily consumed (RACC).

A. Background

Canola oil has the lowest saturated fatty acid (SFA) content (7.1% of total fatty acids) of all vegetable oils commonly consumed in the United States (U.S.) (see Table 1 on page 11). This favorable fatty acid content makes canola oil a valuable food for consumers to help reduce the risk of CHD by lowering serum total cholesterol (T-C) and low density lipoprotein-cholesterol (LDL-C) concentrations. In addition, canola oil contains substantial amounts of other potentially cardioprotective substances including omega-6 (n-6) polyunsaturated fatty acids (PUFAs), alpha-linolenic acid (ALA) and non-glyceride components (e.g., plant sterols, tocopherols). As discussed in detail below, the U.S. Canola Association believes that the totality of credible scientific information supports the following qualified health claim:

[1] Interim Procedures for Qualified Health Claims in the Labeling of Conventional Human Food and Human Dietary Supplements. July 10, 2003. http://www.cfsan.fda.gov/~dms/hclmgui3.html .

> Canola oil (19 grams - about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content, according to supportive but not conclusive research. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories.

B. Regulatory precedent

FDA has provided ample precedent for the proposed claim based on its established health claim policies.

1. T-C and LDL-C are appropriate biomarkers for CHD

FDA has accepted the validity of serum lipids (especially T-C and LDL-C) as biomarkers for CHD and has used this rationale for the approval of several other CHD-related health claims. The preamble to the Interim Final Rule for the health claim on plant sterol/stanol esters and CHD (65 *Federal Register* 54686, 54690, September 8, 2000) states:

> … the agency based its evaluation of the relationship between consumption of plant sterol/stanol esters and the risk of CHD primarily on changes in blood total and LDL-C cholesterol resulting from dietary intervention with plant sterol/stanol ester-containing products. A secondary consideration was that beneficial changes in total and LDL-C cholesterol should not be accompanied by potentially adverse changes in HDL-C cholesterol. This focus is consistent with that used by the agency in deciding on the dietary saturated fat and cholesterol and CHD health claim, §101.75 (56 FR 60727 and 58 FR 2739); the fiber-containing fruits, vegetables, and grain products and CHD claim, §101.77 (56 FR 60582 and 58 FR 2552); the soluble fiber from certain foods and CHD claim, §101.81 (61 FR 296, 62 FR 3584, 62 FR 28234, and 63 FR 8119) and the soy protein and CHD claim §101.82 (63FR 62977 and 64 FR 57700).

2. UFAs are an appropriate "substance" for health claims

Further precedent supporting the proposed claim is provided by the QHC for monounsaturated fatty acids (MUFAs) from olive oil and CHD that FDA authorized on November 1, 2004[2]

[2] http://www.cfsan.fda.gov/~dms/qhc-sum.html#olive.

(hereafter referred to as the "olive oil claim"). FDA accepted the position that MUFAs have hypocholesterolemic properties, when fed in a diet low in saturated fat and cholesterol, and accepted olive oil as a source of these fatty acids. The proposed claim is analogous to the olive oil claim except that the substance is UFAs (MUFAs plus PUFAs) rather than MUFAs alone. Broadening the substance of this claim to UFAs is consistent with the following principles accepted by the agency in allowing the olive oil claim.

a. UFAs have the ability to lower serum T-C and LDL-C by replacing dietary saturated fat

FDA acknowledged that an important consideration in allowing the QHC for olive oil was the ability of MUFAs to lower serum T-C and LDL-C by substituting for a hypercholesterolemic component of the diet (SFAs). Both MUFAs *and* PUFAs from canola oil have an equal capacity to replace dietary SFAs. Therefore, the precedent established by FDA with respect to MUFAs applies equally to UFAs from canola oil – the substance of the proposed claim.

b. UFAs can lower T-C and LDL-C independently of their ability to replace dietary SFAs

The ability of PUFAs to lower serum T-C and LDL-C when they replace carbohydrates in diets containing equal amounts of SFAs has been known since the 1950s (Keys *et.al.*, 1957). More recent data (Yu *et.al.*, 1995; Mensink *et.al.*, 2003) show that MUFAs also have an independent effect on serum lipids. The agency has not revealed the weight given to this mechanism in its decision to allow the olive oil claim; however, PUFAs are even more effective than MUFAs at lowering serum T-C and LDL-C when they replace carbohydrates in diets with the same SFA

content. Therefore, whatever credence FDA placed on the independent ability of MUFAs to affect serum lipids also extends to UFAs from canola oil – the substance of the proposed claim.

3. FDA invited interested parties to petition for a health claim for vegetable oils high in UFAs

FDA's letter allowing the QHC for olive oil discussed comments the agency received suggesting that other oils high in MUFAs and/or PUFAs be permitted to bear the claim. FDA rejected these suggestions because the object of the claim under consideration was MUFAs from olive oil and scientific evidence pertaining to other oils high in UFAs was not provided by the petitioner. However, the agency acknowledged the potential appropriateness of such claims noting, "…vegetable oil manufacturers and others may petition the agency to allow for the use of claims for vegetable oils high in MUFAs and PUFAs relative to saturated fatty acids (SFAs)"[3].

4. FDA authorized a health claim for phytosterols and reduced risk of CHD

Canola oil is the richest source of plant sterols of all MUFA-predominant vegetable oils (see Table 2 on page 22). The primary mechanism by which canola oil reduces the risk of CHD is by exerting favorable effects on serum lipids. Nevertheless, the non-glyceride constituents of this oil may also contribute to its cardioprotective properties. FDA concluded that plant sterols may reduce the risk of CHD in its interim final rule for an unqualified health claim (65 *Federal Register* 54686).

In conclusion, the U.S. Canola Association believes there is strong regulatory precedent for the proposed claim. FDA has authorized the majority of CHD-related health claims on the basis of

[3] http://www.cfsan.fda.gov/~dms/qhcolive.html .

lowering T-C and LDL-C. The precedent established by the QHC for olive oil accommodates broadening the substance of the claim to UFAs (a combination of MUFAs and PUFAs) from canola oil. In addition, FDA has recognized the ability of plant sterols to favorably affect serum lipids. Finally, the agency invited interested parties to submit such a petition for a vegetable oil high in UFAs. The U.S. Canola Association is pleased to respond to this invitation.

C. Prioritization

FDA's guidance document for QHCs provides specific criteria the agency uses in prioritizing the review of such petitions. The U.S. Canola Association believes that this petition satisfies all of these criteria (noted below) and should be given the agency's highest possible priority. Specifically, and as set forth in greater detail in the sections that follow, the proposed claim:

- "is likely to have a significant impact on a serious life-threatening illness" (CHD is the leading cause of death in the U.S. and it would be relatively easy for consumers to substitute canola oil and/or canola oil-containing products for less healthy foods);
- is supported by "strong scientific evidence" (14 of 17 controlled, randomized intervention studies with an FDA quality rating of "+" or "Ø" support the proposed claim);
- consumer research is provided to show that the claim is not misleading;
- the safety of canola oil as a dietary component is unquestioned;
- the substance of the claim (UFAs from canola oil) has been well characterized so that the available studies are relevant and can be evaluated (as was the case for MUFAs from olive oil);
- CHD has been well defined and validated biomarkers for this condition have been accepted by FDA; and

- FDA and other recognized bodies of "qualified experts" (e.g., the National Heart, Lung, and Blood Institute, the Institute of Medicine) have concluded that UFAs can reduce the risk of CHD when included in a moderate-fat diet that is low in SFAs.

Based on these criteria, the U.S. Canola Association urges FDA to move as swiftly as possible to allow use of the proposed claim.

II. PRELIMINARY REQUIREMENTS

Petitions for health claims pertaining to a food component to be consumed at other than decreased dietary levels are required by 21 C.F.R. § 101.70 to provide an explanation of how the substance of the claim conforms to 21 C.F.R. § 101.14(b). The specific requirements of this provision are that the substance is associated with a disease that affects the general U.S. population, contributes nutritive value and/or functionality to food products and is safe and lawful under the federal Food Drug and Cosmetic Act. The U.S. Canola Association contends that the substance of the proposed claim (UFAs from canola oil) meets all of these requirements as discussed below:

A. UFAs from canola oil are associated with a disease affecting the general U.S. population

This petition demonstrates that UFAs from canola oil have the potential to help consumers reduce their risk of CHD. This disease accounted for 53% of all mortality due to cardiovascular disease (CVD) in the U.S. in 2002 (American Heart Association, 2005). CVD is the leading cause of mortality in the U.S. and accounted for 38.0% of all deaths during this year. Nearly 2,600 Americans currently die of CVD each day (an average of one death every 34 seconds), and CVD claims about as many lives each year as the next five leading causes of death combined (cancer, chronic lower respiratory diseases, accidents, diabetes mellitus and influenza/pneumonia). Approximately 1,400,000 death certificates listed CVD as a primary or contributing cause of death in 2002, and the total direct and indirect cost of this disease was estimated to be $395.5 billion (American Heart Association, 2005). Clearly, CHD is a serious public health concern in the U.S.

B. UFAs contribute nutritive value to the diet and functionality to food products

The definition of "nutritive value" under 21 C.F.R. § 101.14 (a)(3) is "a value in sustaining human existence by such processes as promoting growth, replacing loss of essential nutrients, or providing energy." All UFAs provide nutritive value to the diet by serving as a source of energy. Energy is an essential component of the diet and "Estimated Energy Requirements" for different age-gender segments of the population have been established by the Institute of Medicine's (IOM's) Food and Nutrition Board (IOM, 2002). In addition, two of the UFAs found in canola oil (linoleic acid (18:2, n-6) and ALA (18:3, n-3)) are essential nutrients. The Adequate Intake (AI) of linoleic acid for adults ranges from 11g/d for women >70 years of age to 17 g/d for men aged 19-50 (IOM, 2002). Similar values for ALA are 1.1 g/d for women and 1.6 g/d for men 19 years of age and older. Finally, UFAs in the context of the proposed claim are most appropriately considered in a nutritional sense as components of triglycerides. However, UFAs may also be used to provide functionality to food products in their free form or as components of mono-, di- or triglycerides. For example, oleic acid (18:1, n-9) is authorized as a direct food additive under 21 C.F.R. § 172.860 for use as a lubricant, binder and a defoaming agent, which are technical effects that are listed in 21 C.F.R. § 170.3 (o)(14), (18) and (29). In addition, linoleic acid has been authorized for addition to foods as a flavoring agent, adjuvant and nutritional supplement, according to 21 C.F.R. § 184.1065. This information clearly demonstrates that UFAs from canola oil contribute nutritive value and functionality to food products.

C. UFAs are safe and lawful

UFAs are ubiquitous, natural components of the food supply that are both safe and lawful. FDA concluded that MUFAs from olive oil are safe and lawful in the context of its QHC because an

increased intake of the minimum amount deemed necessary for the health benefit (17.5 g/d) would provide only 157 calories, which is well below the IOM's Acceptable Macronutrient Distribution Range (AMDR) for total fat of 25 to 35% of energy (en) (IOM, 2002). In addition, the agency noted that total fat intake would not be expected to increase as a result of the claim because its wording specifies that total calorie intake should not increase.

The reasoning of the olive oil QHC also applies to the proposed claim for canola oil. First, the minimum amount of UFAs necessary to achieve the beneficial effect is similar (17.7 g /d) and language advising constant energy intake has been retained. In addition, modeling studies using data from the 1999-2002 National Health and Nutrition Examination Survey (NHANES) (see section III. F., page 61) confirm that the total fat content of the diet would not change if canola oil replaced soybean, corn, cottonseed, safflower and sunflower oils and if canola oil-based margarine replaced butter and other margarines. Furthermore, such a replacement would have positive effects on the number of individuals who fall within the AMDR for n-6 PUFAs and who meet the AI for ALA. Finally, as noted above, oleic acid and linoleic acid have been authorized as direct food additives under 21 C.F.R. § 172.860 and 21 C.F.R. § 184.1065, respectively. This information clearly demonstrates that UFAs from canola oil are safe and lawful.

III. SUMMARY OF SCIENTIFIC DATA

A. Credible scientific evidence exists to support the claim

The totality of publicly available scientific evidence provides strong support for the proposed claim. A comprehensive review of the scientific literature as well as recommendations from governmental and professional organizations demonstrates that diets rich in UFAs are well accepted as a means to reduce the risk of CHD. As discussed in detail below, the U.S. Canola Association believes that there is an abundance of credible scientific data to show that:

> Canola oil (19 grams – about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content, according to supportive but not conclusive research. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories.

FDA acknowledged the importance of MUFAs in this regard with the authorization of the olive oil claim.[4] In addition, the ability of dietary PUFAs to reduce the incidence of CHD has been widely recognized (National Cholesterol Education Program, 2002; Sacks and Katan, 2002). This information shows that UFAs (the combination of MUFAs and PUFAs) are an appropriate substance for the proposed claim.

The data presented in Table 1 show that canola oil has the highest concentration of UFAs of all edible oils in the U.S. with disappearance of greater than 100 million pounds per year. The UFAs in canola oil are composed of a unique blend of MUFAs as well as n-6 and n-3 PUFAs. In addition, non-glyceride components of canola oil (Phillips *et.al.*, 2002), including phytosterols (e.g., brassicasterol, campesterol, β-sitosterol) and several forms of tocopherol, (Pruthi *et.al.*, 2001) may enhance its cardioprotective effects.

[4] http://www.cfsan.fda.gov/~dms/qhcolive.html .

Table 1
U.S. Disappearance and Fatty Acid Content of Edible Oils

Oil	2004 U.S. Disappearance (millions of pounds)*	Fatty acid content (g/100g)**			
		Total Saturated	Total MUFA	Total PUFA	α-Linolenic Acid
Butter	n/a	51.4	21.0	3.0	0.3
Canola	**1,598**	**7.1**	**58.9**	**29.6**	**9.3**
Coconut	879	86.5	5.8	1.8	0
Corn	1,683	12.9	27.6	54.7	1.2
Cottonseed	834	25.9	17.8	51.9	0.2
Flaxseed	n/a	9.4	20.2	66.0	53.3
Lard	917	39.2	45.1	11.2	1.0
Olive	538	13.5	73.9	10.0	0.8
Palm	631	49.3	37.0	9.3	0.2
Palm Kernel	522	81.5	11.4	1.6	0
Peanut	250	16.9	46.2	32.0	0
Safflower (>70% oleic)	88	6.2	74.6	14.4	0
Sesame	24	14.2	39.7	41.7	0.3
Soybean	17,300	14.4	23.3	57.9	6.8
Sunflower (high oleic)	245	9.7	83.6	3.8	0.2

*Source: USDA Economic Research Service, *Oil Crops Yearbook*/OCS-2005, 3/21/05
** Source: USDA National Nutrient Database for Standard Reference, Release 17

The hypocholesterolemic effect of canola oil (when fed as a replacement for SFAs) has been demonstrated by 18 controlled human intervention studies (including nine that meet FDA's criteria as "highly persuasive"). Furthermore, five studies have shown that canola oil is as good as or better than olive oil in lowering serum T-C and/or LDL-C concentrations in healthy humans.

Based on these observations, the U.S. Canola Association strongly believes that the weight of available credible scientific evidence demonstrates that UFAs from canola oil reduce the risk of CHD and urges the agency to move swiftly to allow the proposed claim.

B. Scientific evidence demonstrates the public health benefits of UFAs from canola oil

There are several different mechanisms by which the UFAs (and possibly other constituents) in canola oil reduce the risk of CHD. These mechanisms provide the scientific basis for the proposed claim.

1. UFAs lower serum lipids when they replace dietary SFAs and *trans* fatty acids (TFAs)

The hypercholesterolemic properties of SFAs and TFAs are well recognized. Early studies (Ahrens *et.al.*, 1957; Keys *et.al.*, 1957, 1957a) found that both MUFA- and PUFA-rich oils decrease serum T-C and LDL-C (referred to as β-lipoprotein at the time) when they replace SFAs in the diets of human subjects. SFAs (and TFAs) are hypercholesterolemic and replacement of these fatty acids with virtually any other dietary component (including MUFAs, PUFAs or carbohydrates (CHOs)) results in a net decrease in blood T-C and LDL-C concentrations.

Hegsted *et.al.* (1965) reported that SFA intake accounted for 72% of the variation in serum T-C among institutionalized men fed SFA-, MUFA- or PUFA-rich diets. Clark *et.al.* (1997) conducted a meta-analysis of 395 dietary experiments among 129 groups of individuals and concluded that replacement of 5% of calories from SFAs with 5% of calories from PUFAs, while holding total CHO and other dietary components constant, decreased blood T-C by 0.39 mmol/l. A similar replacement of SFAs with MUFAs decreased T-C by 0.24 mmol/l.

Similar results were reported by Gardner and Kraemer (1995) in a meta-analysis of 14 studies. Seven of the studies included in this analysis permitted assessment of the effect of replacing SFAs with either MUFAs or PUFAs while holding other macronutrients constant. Both categories of fatty acids had similar effects on the change in blood LDL-C concentrations. An advisory report from the American Heart Association Nutrition Committee (Kris-Etherton, 1999) confirmed the equivalence of MUFAs and PUFAs when fed as a substitute for SFAs. This report concluded, "Thus, the effects of MUFA versus PUFA substitution for dietary SFA are comparable."

The data from human intervention studies cited above clearly show that replacing SFAs with MUFAs or PUFAs reduces serum T-C and LDL-C concentrations. This observation is consistent with data from the Nurses' Health Study (Hu *et.al.*, 1999), which show that higher intakes of SFAs and TFAs are associated with increased risk of CHD, while higher intakes of MUFAs and PUFAs are associated with reduced risk of this disease.

In summary, one of the mechanisms by which the UFAs in canola oil reduce the risk of CHD is by replacing SFAs in the diet, which favorably affects serum lipids. Both MUFAs and PUFAs are similarly effective in this regard. Canola oil has the highest concentration of UFAs of all edible oils commonly consumed in the U.S. (see Table 1 on page 11).

2. PUFAs and MUFAs have beneficial effects on serum lipids independent of their ability to replace SFAs

Early equations developed to explain the effect of fatty acids on serum lipids clearly showed that SFAs are hypercholesterolemic and that PUFAs lower serum T-C and LDL-C. The first such

equation was published by Keys *et.al.* (1957): Δ T-C = -1.68 + 2.76 ΔS +0.05 ΔM -1.35 ΔP where ΔT-C is cholesterol in mg/dl, ΔM is the change in percent of calories in the diet from MUFAs and ΔP is the change in percent of calories from PUFAs. Hegsted (1986) published a similar equation that included a variable for dietary cholesterol: ΔT-C = 2.16 ΔS – 1.65 ΔP + 0.097 C where ΔS and ΔP have the same meanings as above and ΔC is the difference in cholesterol intake in mg/1,000 kcal. These equations compared the effect of substituting fatty acids in the diet for *CHOs* rather than for each other as discussed in the previous section. These equations show that serum T-C and LDL-C decrease as dietary PUFAs increase at a constant level of SFA intake. In other words, dietary PUFAs exert a hypocholesterolemic effect that is independent of their ability to replace SFAs in the diet.

These early investigators (Keys *et.al.*, 1957; Hegsted, 1986) also concluded that MUFAs do not significantly affect serum lipids when fed as a replacement for CHOs. However, subsequent analyses of lipid feeding studies showed that MUFAs do have an independent effect on serum lipids if the effect of individual SFAs is considered. The following regression equations developed by Yu *et.al.* (1995) considered the effect of stearic acid separately from all other SFAs:

- ΔT-C (mmol/l) = 0.0522*(Δ12:0 – 16:0) – 0.0008Δ18:0 – 0.0124**ΔMUFA – 0.0248*ΔPUFA
- ΔLDL-C (mmol/l) = 0.0378*(Δ12:0 – 16:0) + 0.0018Δ18:0 – 0.0178*ΔMUFA – 0.0248*ΔPUFA
- ΔHDL-C (mmol/l) = 0.0160*(Δ12:0 – 16:0) – 0.0016Δ18:0 + 0.0101*ΔMUFA + 0.0062*ΔPUFA

  where Δ12:0 – 16:0 are the changes in lauric, myristic and palmitic fatty acids when substituted for carbohydrate, Δ18:0 is the change in stearic acid, and ΔMUFA and ΔPUFA are the changes in these classes of fatty acids.

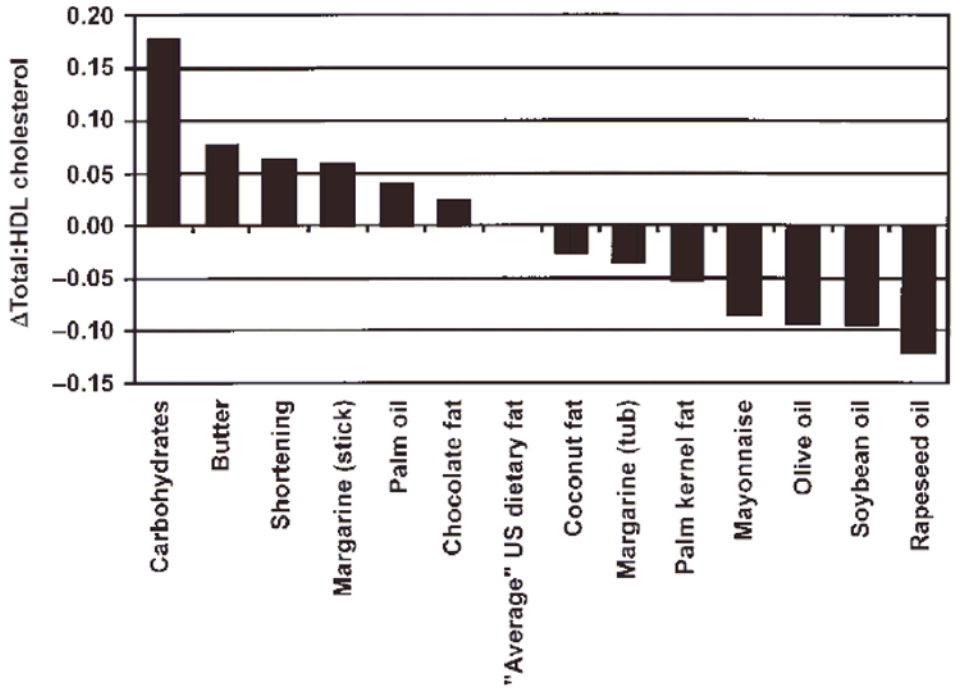
  *regression coefficient different from 0 at $p<0.05$
  ** regression coefficient different from 0 at $p<0.01$

These equations show that the shorter chain SFAs are hypercholesterolemic when fed in place of CHOs, but that stearic acid is neutral. In addition, the regression coefficients for MUFAs and PUFAs are negative and significantly different from zero with respect to T-C and LDL-C, which demonstrates that both classes of UFAs lower serum lipids independent of their ability to substitute for SFAs. In addition, both MUFAs and PUFAs have positive regression coefficients with respect to HDL-C, which indicates that these classes of UFAs have a beneficial effect on this lipid component. The authors concluded:

> Based on our results we speculate that the effect of MUFAs on serum total cholesterol and LDL-C is dependent on the amount of SFA (and specifically the amount of hypercholesterolemic SFA) in the diet. Based on this line of reasoning, when 12:0 – 16:0 SFAs in the diet are low, the independent cholesterol-lowering effect of MUFAs is observed. In contrast when 12:0 – 16:0 SFAs are high, the cholesterol-lowering effect of MUFAs is obscured, and MUFAs appear to have a neutral cholesterolemic effect.

Similar results were reported by Mensink *et.al.* (2003) who found negative regression coefficients for MUFAs and PUFAs in equations analogous to those shown above for ΔLDL-C derived from a meta-analysis of 60 feeding studies. As in the analysis of Yu *et.al.* (1995), these investigators found that both MUFAs and PUFAs significantly increased serum HDL-C concentrations and lowered the T-C/HDL-C ratio when fed in place of CHOs. The predicted changes on this ratio when CHOs or various sources of fat replace mixed fats in the average American diet at 10% of total energy are presented in Figure 1. This figure shows that low erucic acid rapeseed oil (canola oil) is predicted to have the most beneficial effect on the T-C/HDL-C ratio compared to several commonly consumed fats (including olive oil) and CHOs.

Figure 1
Effect of Replacing Mixed Fat in the Average American Diet with Carbohydrate or Various Fat Sources at 10% of Total Energy



Source: Mensink, R.P *et.al.* 2003. *Am. J. Clin. Nutr.* 77:1146

In summary, the available data show that both MUFAs and PUFAs have beneficial effects on serum lipids *independent* of their ability to replace SFAs in the diet. Canola oil has the highest PUFA content of all MUFA-predominant oils commercially available in the U.S. (including olive oil).

3. PUFAs reduce the incidence of CHD

Randomized controlled intervention studies with "hard" clinical endpoints have shown that dietary PUFAs reduce the incidence of CHD compared to diets higher in SFAs (National Cholesterol Education Program, 2002; Sacks and Katan, 2002). Unfortunately, rigorously controlled,

randomized intervention studies using MUFAs as a substitute for SFAs have not been reported (National Cholesterol Education Program, 2001).

The most rigorous of these trials (Dayton *et.al.*, 1969) was a randomized, placebo-controlled, double-blind feeding study among 846 male subjects (mean age = 65.5 years). The experimental group was given a diet in which one or more PUFA-rich oils (i.e., corn, soybean safflower or cottonseed) replaced sources of SFAs. The PUFA content of the control and experimental diets was 5.5% and 17% of energy, respectively. The control diet had 19% of energy as SFAs compared to 8% for the experimental diet, and the MUFA content of the two diets was similar (15-16%). Seven percent of both the control and experimental groups had a previous myocardial infarction (MI) and 12% in each group had a history of angina, but the majority of these subjects were free of apparent CHD at baseline. The follow-up period was eight years. The experimental group had 31% fewer ($p=0.01$) total cardiovascular endpoints compared to the control group and the combined incidence of MI, sudden death and stroke was reduced by 34% ($p=0.04$).

Other controlled feeding studies that reported a significant reduction in the incidence of CHD when PUFA-rich diets were compared to higher SFA-containing diets included the Oslo Diet-Heart Study (Leren, 1970) among 412 male patients aged 30 to 64 years who had experienced a prior MI and the Finnish Mental Hospital Study (Turpeinen *et.al.*, 1979), which reported reduced incidence of CHD among 676 hospitalized mental patients during a 12-year cross-over study. A fourth controlled study (Research Committee, 1968) found that 199 male MI patients given high-PUFA diets had fewer fatal or non-fatal recurrent events than 194 control patients (45 vs. 51), but the results were not statistically significant.

In summary, randomized intervention studies with hard clinical endpoints provide compelling evidence that PUFA-rich diets reduce the risk of CHD. These data are also consistent with numerous studies that show PUFAs have favorable effects on serum lipids. Canola oil has the highest PUFA content of all MUFA-predominant oils commercially available in the U.S. (including olive oil).

4. Alpha-linolenic acid may be cardioprotective

The relationship between n-3 fatty acids (i.e., docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and ALA) and CHD has been the subject of several recent review papers (Kris-Etherton *et.al.*, 2002; de Lorgeril and Salen, 2004; Wang *et.al.*, 2004; Wijendran and Hayes, 2004; Mozaffarian, 2005; Schmidt *et.al.*, 2005, 2005a).

Long-chain n-3 fatty acids (i.e., DHA and EPA) are becoming increasingly recognized for their cardioprotective potential in healthy individuals (Kris-Etherton *et.al.*, 2002; Wang *et.al.*, 2004). Nevertheless, considerable evidence suggests that ALA (a shorter chain n-3 fatty acid) is also beneficial. Wijendran and Hayes (2004) noted that ALA may have beneficial effects on cardiac arrhythmia, inflammation or thrombosis. Mozaffarian (2005) echoed this observation and concluded that while the predominance of available data (primarily from epidemiologic studies) suggest that ALA reduces the risk of CHD, more controlled intervention studies are needed to make definitive conclusions. Results of the prospective observational studies and an intervention trial in this area are summarized below.

Dolecek (1992) reported that dietary ALA was inversely associated with mortality from CHD ($p<0.05$) and all-cause mortality ($p<0.05$) among 6,250 members of the Multiple Risk Factor Intervention Trial cohort.

Ascherio *et.al.* (1996) found that ALA intake was inversely associated with the incidence of MI (but not with fatal MI) among a large cohort of male health professionals followed for an average of 10 years. A one percent increase in ALA intake was associated with a 41% reduction in non-fatal MI (95% Confidence Interval (CI), 21-80%) after adjustment for multiple CHD risk factors, including dietary fiber. There was also an inverse association with nonfatal MI that was not statistically significant after adjustment for possible confounding variables (Relative Risk (RR)=0.57; 95% CI, 0.18-1.79).

Pietinen *et.al.* (1997) found no association between the incidence of fatal or non-fatal CHD and ALA intake among 21,930 members of the Alpha-Tocopherol, Beta-Carotene Cancer Prevention study cohort after 6.1 years of follow-up. However, this study also failed to detect an association between CHD and other fatty acid classes believed to be associated with this disease (i.e., SFAs, n-6 PUFAs, MUFAs).

ALA intake was associated with reduced risk of CHD in a prospective cohort study of 76,286 female nurses (Hu *et.al.*, 1999a). Subjects in the highest quintile of ALA intake were less likely to experience fatal ischemic heart disease compared to those in the lowest quintile (RR=0.55; 95% CI, 0.32 – 0.94) after adjusting for numerous CHD risk factors. A similar trend (RR=0.85; 95% CI, 0.61 – 1.19) was detected for nonfatal ischemic heart disease.

Baylin *et.al.* (2003) found that Costa Rican subjects in the top quintiles of adipose tissue ALA were significantly less likely to experience a first nonfatal acute MI compared to individuals in the lowest quintile (RR = 0.31; 95% CI, 0.24 – 0.59) in a nested case-control study of 482 patients and a similar number of healthy controls. This association was strengthened after adjustment for MI risk factors, including smoking, physical activity, income, adipose tissue linoleic acid and TFA concentrations.

Lemaitre *et.al.* (2003) found that a one-standard deviation increase in the concentration of plasma phospholipid ALA was associated with a decrease in fatal (RR = 0.48; 95% CI, 0.24 – 0.96) but not nonfatal (RR = 1.07; 95% CI, 0.81 – 1.41) ischemic heart disease among 54 cases and an equal number of controls after adjustment for potentially confounding variables. The subjects were members of the Cardiovascular Health Study cohort.

Dietary ALA was inversely associated with total mortality (RR = 0.85; p for trend = 0.01) among 41,836 members of the Iowa Women's Health Study after 442,965 person-years of follow-up (Folsom and Demissie, 2004). The longer chain n-3 fatty acids (i.e., DHA and EPA) were not associated with mortality in this cohort.

Albert *et.al.* (2005) reported that incidence of sudden cardiac death was inversely associated (RR = 0.60; p for trend = 0.02) with ALA intake among 76,763 women in the Nurses' Health Study after 18 years of follow-up. The data were adjusted for age, energy intake, smoking status, BMI, alcohol intake, menopausal status, use of hormone replacement therapy, aspirin use, multivitamin use, vitamin E supplement use, history of hypertension, hypercholesterolemia, diabetes, family

history of MI, history of prior CVD, TFA intake and ratio of dietary PUFA to SFA and n-3 fatty acid intake. There were no associations between ALA intake and other types of fatal CHD or nonfatal MI.

A meta-analysis (Brouwer *et.al.*, 2003) of prospective cohort studies concluded that ALA intake is associated with reduced incidence of fatal heart disease (RR=0.79; 95% CI, 0.6-1.04), however, a positive association with prostate cancer was also observed[5].

Only one randomized, controlled dietary intervention study has been conducted to investigate the effect of ALA on CHD (Singh *et.al.*, 1997). Subjects who had suffered an acute MI were given 2.9 g/d ALA (from mustard oil), a combination of 1.08 g EPA and 0.72 g DHA/day or a placebo. Nonfatal infarctions ($p<0.05$) and total cardiac events ($p<0.01$) were reduced in the ALA and fish oils groups, but fatal cardiac events were only different ($p<0.01$) in the fish oil group. The results of this study are encouraging for both long- and short-chain n-3 fatty acids; however, use of MI patients limited the conclusions that can be made for the normal, healthy population.

Finally, an American Heart Association Scientific Statement on the role of n-3 fatty acids and CHD (Kris-Etherton *et.al.*, 2002) concluded:

> Collectively, these data are supportive of the recommendation made by the AHA Dietary Guidelines to include at least two servings of fish per week (particularly fatty fish). In addition, the data support inclusion of vegetable oils (e.g., soybean, canola, walnut, flaxseed) and food sources (e.g., walnuts, flaxseeds) high in α-linolenic acid in a healthy diet for the general population.

[5] The possible association between ALA intake and prostate cancer has been questioned by Attar-Bashi *et.al.* (2004, 2004a).

In summary, there is considerable evidence that adequate intake of n-3 fatty acids reduces the risk of CHD. The data are stronger for the long-chain forms, but substantial observational data suggest that ALA may also be effective. Canola oil has the highest ALA content (9.3%) of all commonly consumed oils in the U.S. (including olive oil; 0.8%) and this component may contribute to its cardioprotective properties.

5. Other constituents in canola oil may be cardioprotective

Canola oil has a variety of other constituents that may contribute to its cardioprotective properties.

a. Plant sterols

Canola oil contains more phytosterols than any other MUFA-predominant oil, and is surpassed only by corn oil (a PUFA-predominant oil) as a source of these constituents (Phillips *et.al.*, 2002). The distribution of major sterols in canola oil compared to other commonly consumed oils in the U.S. is presented in Table 2.

Table 2
Concentration of Total Free and Esterified Phytosterols in Select Edible Oils (mg/100g)

Sterol	Canola	Corn	Cotton seed	Olive	Palm	Peanut	Soy	Sunflower
Brassicasterol	**46.7**	0	0	0	0	1.2	0.2	2.1
Campesterol	**208**	263	20.2	4.3	7.3	23.7	45.5	27.1
Campestanol	**1.7**	19	0.9	0.7	1.2	0.9	2.2	1.2
Stigmasterol	**142**	121	5.0	2.5	8.0	12.0	49.1	17.7
β-Sitosterol	**377**	1,348	256	126	39.5	115	141	194
Δ5-Avenasterol	**22.4**	339	7.5	16.7	14.2	12.9	5.8	18.7
Sitostanol	**2.7**	30	2.9	3.1	3.5	2.5	4.2	2.9
Total (mg/100g)	**800.5**	2,120	292.5	153.3	73.7	168.2	248	263.7

Source: Phillips *et.al.* 2002. Free and Esterified Sterol Composition of Edible Oils and Fats *J Food Comp. Anal.* 15:123.

Plant sterols and stanols are hypocholesterolemic because they reduce the absorption of cholesterol (Ostlund, 2004). A recent meta-analysis of 41 intervention trials (Katan *et.al.*, 2003) found that daily consumption of 2g/d of plant sterols or stanols reduces LDL-C concentrations by approximately 10%. However, much lower doses (0.7-1.1 g/d) also prompt a significant reduction (6.7%, $p<0.05$) in this biomarker. These data have prompted the National Cholesterol Education Program (2001) and the American Heart Association (Krauss *et.al.*, 2000) to acknowledge the potential value of phytosterols in the management of CHD. Canola oil has the potential to make a contribution to the total intake of these substances as part of a balanced diet.

b. Tocopherols

Canola oil meets the current definition of good source of vitamin E (4.8 IU per RACC; ~16% DV). In addition, canola oil contains substantial amounts of γ-tocopherol (8.5 mg/RACC) and traces of δ-tocopherol (0.28 mg/RACC)[6].

The effect of vitamin E and other tocopherols on CHD incidence has not been completely determined. Most observational studies (Rimm *et.al.,* 1993; Kushi *et.al.*, 1996), but not all, (Muntwyler *et.al.*, 2002) have shown that vitamin E supplement use is associated with decreased risk of CHD. However, the majority of randomized clinical trials have not found a beneficial effect of this nutrient among healthy individuals (The Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group, 1994; Hennekens *et.al.*, 1996; Vivekananthan *et.al.*, 2003). The significance of the largely negative findings of the intervention studies has been questioned (Steinberg and Witztum, 2002; Griendling and FirzGerald, 2003) due to the possibility of inappropriate endpoints, inappropriate subjects, ineffective test compounds and other factors.

[6] USDA National Nutrient Database for Standard Reference, Release 17.

Oxidation of LDL-C is widely recognized as an early step in the atherosclerotic process (Lusis, 2000). It is possible that antioxidants in foods (including mixed tocopherols) are more cardioprotective than purified vitamin E provided as dietary supplements (Krauss *et.al.*, 2000).

* * *

In conclusion, the U.S. Canola Association believes that there is strong scientific rational to support the proposed claim. The UFAs in canola oil are capable of lowering T-C and LDL-C by replacing SFAs in the diet and through an independent mechanism unrelated to SFA intake. Canola oil also contains substantial amounts of ALA that may protect against CHD by preventing arrhythmias or by acting through other mechanisms unrelated to serum T-C and LDL-C concentrations. Finally, canola oil is a source of non-glyceride components, including phytosterols and tocopherols, which may augment its ability to reduce the risk of CHD in healthy individuals.

C. Scientific publications on UFAs from canola oil and CHD

As previously discussed, MUFAs and PUFAs have been shown to reduce serum T-C and LDL-C concentrations when fed to healthy human subjects as a replacement for dietary SFAs. In addition, these UFAs have independent effects on blood lipids when fed in diets of equal SFA content. The purpose of this section is to review the individual scientific publications pertaining to canola oil as a source of UFAs. Studies that examined UFA sources other than canola oil are not discussed in this document because FDA did not consider such studies relevant in its assessment of the olive oil claim[7]. The U.S. Canola Association believes that the overwhelming weight of credible scientific evidence discussed below supports the proposed claim.

[7] http://www.cfsan.fda.gov/~dms/qhcolive.html .

In accordance with 21 C.F.R. § 101.70(c) and 21 C.F.R. § 170(d), the U.S. Canola Association declares that to the best of its knowledge, all non-clinical studies relied upon in this petition were conducted in compliance with the good laboratory practice regulations set forth in 21 C.F.R. Part 58. Moreover, all clinical or other human investigations relied upon were either conducted in accordance with the requirements for institutional review set forth in 21 C.F.R. Part 56 or were not subject to such requirements in accordance with 21 C.F.R. §§ 56.104 or 56.105, and were conducted in compliance with the requirements for informed consent set forth in 21 C.F.R. Part 50.

1. Observational studies

No observational studies were identified that investigated the possibility of an association between canola oil intake *per se* and the risk of CHD.

Eight observational studies were found that examined the association between intake of total MUFAs and/or PUFAs and one or more CHD-related parameters. Four of these studies (Keys *et.al.*, 1986; Trevisan *et.al.*, 1990; Hu *et.al.*, 1997; Kouris-Blazos *et.al.*, 1997) reported inverse associations between the intake of UFAs and parameters of CHD, while the remaining studies found a direct association (Posner *et.al.*, 1991; Esrey *et.al.*, 1996; Suh *et.al.*, 2001) or no association (Trichopoulou *et.al.*, 2003).

These studies will not be discussed in detail because they do not pertain specifically to canola oil. In addition, the agency's "Interim Evidence-based Ranking System for Scientific Data" states that dietary intervention studies are much more persuasive than observational studies with respect to

the substantiation of health claims[8]. Furthermore, FDA did not rely on observational studies in deciding to allow the QHC for olive oil[9]. Nevertheless, in the interest of completeness, the studies cited above are appended to this petition to provide the agency with the totality of scientific evidence in this area.

In conclusion, the U.S. Canola Association agrees with FDA's decision to place considerable emphasis on controlled intervention studies for the substantiation of health claims when they are available. The conclusions that can be drawn from the observational studies with respect to UFAs from canola oil and risk of CHD are limited by several factors. Some of the available studies are of poor quality. In addition, the fatty acid composition of diets is more difficult to accurately assess than the intake of individual foods, the influence of uncontrolled confounding variables cannot be eliminated and epidemiologic studies are inherently incapable of proving causality.

2. Intervention studies

A review of the criteria FDA has used to identify intervention studies that are germane to CHD-related health claims was described in the interim final rule for the sterol/stanol ester health claim (65 *Federal Register* 54686 at 54691). These criteria include:

> …(1) Present data and adequate descriptions of the study design and methods; (2) be available in English; (3) include estimates of, or enough information to estimate, intakes of plant sterols or stanols and their esters; (4) include direct measurement of blood total cholesterol and other blood lipids related to CHD; and (5) be conducted in persons who represent the general U.S. population. In the case of criterion (5), these persons can be considered to be adults with blood total cholesterol levels less than 300 mg/ dL, as explained below.

[8] http://www.cfsan.fda.gov/~dms/hclmgui4.html .
[9] http://www.cfsan.fda.gov/~dms/qhcolive.html .

The minimum level of reduction in T-C or LDL-C that the agency considers necessary for the authorization of a health claim has not been rigidly defined. However, a decrease in total cholesterol of 4.4 percent (10.0 milligrams mg/dL) and in LDL-C of 4.9 percent (7.8 mg/dL) was regarded as significant in authorizing a health claim for oats and coronary heart disease (62 *Federal Register* 3584, 3586, January 23, 1997), and similar levels were used to justify authorization of a health claim for soy protein and CHD (64 *Federal Register* 57700, 57708, October 26, 1999).

The landmark report, *Diet and Health* (National Academy of Sciences, 1989), was a comprehensive review of the relevant scientific literature. This report provides direct support for the proposed claim by concluding that MUFAs and n-6 PUFAs lower LDL cholesterol when substituted for SFAs. The *Diet and Health* report was also used as a benchmark in support of the QHC for olive oil. It is, therefore, not necessary to review individual studies cited in this report. All dietary intervention studies published since the NAS *Diet and Health* report that examined the effect of canola oil on serum lipids in healthy human subjects are discussed in chronological order below and summarized in tabular form in Appendix A.

The studies described below are also rated for quality using the following criteria provided by FDA in its July 10, 2003 guidance document[10] "Interim Evidence-based Ranking System for Scientific Data":

- (+) means the report has adequately addressed issues of scientific quality such as inclusion/exclusion, bias, generalizability, and data collection and analysis.

[10] http://www.cfsan.fda.gov/~dms/hclmgui4.html .

- (Ø) means some uncertainties exist as to whether the report has adequately addressed issues of scientific quality such as inclusion/exclusion, bias, generalizability, and data collection and analysis.

- (-) means the report has not adequately addressed issues of scientific quality such as inclusion/exclusion, bias, generalizability, and data collection and analysis.

- N/A means the report is not a primary reference, therefore, the quality has not been assessed, and such a reference is not considered as part of the body of evidence on which the final ranking is based. Examples of non-primary references are review articles and meta analyses.

The quality ratings assigned to the studies discussed in this section are based exclusively on their ability to provide evidence germane to the proposed claim. In some cases, these studies were designed for a different purpose; hence, their quality rating may have been different if applied to the original purpose. Studies that compared diets containing canola oil to those rich in SFAs are discussed separately from studies that compared canola oil to olive oil.

a. Studies that compare canola oil-containing diets with those higher in SFAs

Baudet *et.al.* (1988)[11] examined the effect of diets that provided 15.6 percent of energy (% en) as low erucic acid rapeseed oil (equivalent to canola oil), milk fat, sunflower oil or peanut oil on serum lipids using a randomized, cross-over design with six-week intervention periods. The subjects were 20 healthy nuns living in a Benedictine monastery (mean age = 39 years) who had normal serum lipid values at baseline (T-C = 208 mg/dl; LDL-C = 137 mg/dl; HDL-C = 69 mg/dl). The subjects had consumed the same diet for several years before the start of the experiment and "rigorously applied the dietary instructions." The average energy content of all diets was 2,000

[11] This study was published prior to the NAS *Diet and Health Report* but is discussed here because it was not cited in that document.

kcal/d and the macronutrient distribution was similar (total fat 30% en; CHO 54% en; protein 30% en). The cholesterol content of the high SFA diet was 400 mg/d compared to 300 mg/d for the other three diets. The fatty acid distribution (% weight of total fatty acids of SFAs, MUFAs and PUFAs) for the high SFA diet was 70%, 27.8% and 2.2%, respectively. Analogous data for the canola oil diet were 7.0%, 58.4% and 33.4%, respectively. Serum T-C (185 mg/dl) and LDL-C (114 mg/dl) after the canola oil diet were significantly lower ($p<0.01$) than after the SFA diet (T-C = 223 mg/dl; LDL-C = 148 mg/dl). The percent decreases in serum T-C and LDL-C were 17% and 23%, respectively. There were no significant changes in HDL-C between these two sources of fat. The canola oil diet also resulted in lower ($p<0.01$) blood T-C than the sunflower oil diet and in lower ($p<0.01$) LDL-C than the sunflower and peanut oil diets. Body weight did not change during the study. This paper provides strong evidence that canola oil has a favorable effect on serum lipids when compared to diets higher in SFAs. The experimental diets were very similar in macronutrient content, but there was a 100 mg/d difference in cholesterol. According to equations[12] derived by Hegsted *et.al.* (1993), the theoretical effect of this difference in cholesterol intake on serum T-C and LDL-C was 3.35 and 2.2 mg/dl, respectively. These differences are small compared to the observed decrease in serum T-C (-38 mg/dl) and LDL-C (-34 mg/dl) concentrations between the canola oil and SFA diets. The percent decrease in serum T-C would change only slightly (from -17% to -15.5%) after adjustment for the theoretical effect of dietary cholesterol. Similar adjustment for the percentage decrease in LDL-C (from -23% to -21.5%) is

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[12] * ΔT-C (mg/dl) = 2.10ΔS -1.16ΔP + 0.067ΔC

* ΔLDL-C (mg/dl) = 1.74ΔS -0.766ΔP + 0.439ΔC

where ΔS and ΔP are % en of dietary SFAs and PUFAs, respectively and Δ is dietary cholesterol expressed as mg/1,000 kcal.

also small. These changes do not materially alter the conclusions of the study, which provides strong, credible support for the proposed claim. **[FDA quality rating +]**

A randomized, cross-over design protocol was used by McDonald *et.al.* (1989) to study the effect of canola and sunflower oils on blood lipids among eight normocholesterolemic (baseline serum T-C = 3.08 – 4.82 mmol/l) male subjects aged 19 to 23 years. A mixed fat baseline diet was fed for six days before and after the experimental periods. The subjects were randomized to one of the two experimental diets for 18 days. The test fats accounted for approximately 75% of total fat, which comprised 28% of total energy. All diets (including the mixed fat diet) provided approximately 3,000 kcal/d, 28% en fat, 49.5% en CHO and 14.5% en protein. The cholesterol intake was not reported, but it was probably somewhat higher on the mixed fat diet because this diet contained butter and other sources of animal fat. The mixed fat diet provided 14% en SFAs, 15% en MUFAs and 7% en PUFAs. Analogous data for the canola oil diet was 5%, 20% and 10% en, respectively. Data for the two experimental periods in this cross-over study were presented separately. Mean differences for the canola oil treatment compared to the mixed fat diet for the first period showed a decrease in T-C (-20.1, $p<0.05$), LDL-C (-25.2%, $p<0.05$) and HDL-C (-10.6%, $p<0.05$). Analogous data for the second experimental period were T-C (-15.2%, $p<0.05$), LDL-C (-22.4%, NSD) and HDL-C (-5.0%, NSD). Serum T-C and LDL-C concentrations decreased more than that of HDL-C, so the overall effect on serum lipids was beneficial. There were no significant differences between the canola and sunflower oil groups. Body weight data were not presented, but the paper noted that energy intakes were adjusted to avoid weight changes. The small number of subjects in this study and marginal treatment duration (slightly less than three weeks) limit the conclusions that can be drawn. In addition, the lack of cholesterol intake data

prevents estimating the effect of this compound on serum lipid results. Nevertheless, the macronutrient content of the diets was tightly controlled and canola oil caused large reductions in serum T-C and LDL-C. This study provides suggestive support for the proposed claim. **[FDA quality rating Ø]**

Wardlaw *et.al.* (1991) studied the effect of a diet rich in canola or safflower oil compared to a high SFA butter-containing diet among 32 moderately hypercholesterolemic (serum T-C > 5.17 mmol/l) male subjects (mean age = 33 years). The subjects were randomized to one of the test diets for eight weeks after consuming a high SFA baseline diet for three weeks using a single-blind, parallel design. The test fats in all three diets provided approximately 80% of total fat. The diets contained 39% en total fat and were similar in CHO, protein and alcohol content. The high SFA diet contained slightly more cholesterol (360 mg/d) than the experimental diets (320 mg/d). The fatty acid content of the diets for SFAs, MUFAs and PUFAs were 15%, 14% and 9% en, respectively for the high SFA diet and 7%, 22% and 11% en, respectively for the canola oil group. Three subjects failed to complete the study after randomization. The canola oil group experienced significant reductions in blood T-C (-9%, $p<0.01$) and LDL-C (-12%, $p<0.01$) concentrations compared to the SFA group. There was no significant difference between the two diets on serum HDL-C (+1% on the canola diet). Safflower oil feeding also resulted in significant decreases in serum T-C and LDL-C with no significant difference in HDL-C. The slight difference in cholesterol between the SFA and experimental diets (13.6 mg/1,000 kcal) would not have a meaningful effect on serum lipids based on the equations used above (Hegsted *et.al.*, 1993). The theoretical difference in both serum T-C and LDL-C due to differences in cholesterol intake was 0.02 mmol/l. This difference constitutes only 4.2% of the 0.47 mmol/l drop in serum T-C

observed between the SFA-rich and canola-containing diets and only 4.6% of the 0.43 mmol/l decrease between these two diets for serum LDL-C. Body weights did not change during the experiment. This study provides strong, credible evidence that canola oil has a favorable effect on blood lipids when compared to diets higher in SFA. **[FDA quality rating +]**

Seppänen-Laakso *et.al.* (1992) used a randomized, parallel design with a six-week intervention period to compare the effect on blood lipids of replacing butter in the diet with rapeseed (canola) oil or a margarine containing mixed fat sources. A control group of mixed fat users was also included to monitor changes in serum lipids during the experiment. Fifty-four moderately hypercholesterolemic (mean baseline serum T-C = 6.32 mmol/l) men and women (28 females) with a mean age of approximately 43 years participated in the study. The subjects were randomized alphabetically to a canola (n=20), margarine (n=23) or control (n=11) group after consuming the baseline diet for six weeks. The canola oil group consumed approximately 18 g/d of the test fat (20% en). There were no significant differences in energy, total fat (39-40% en), CHO, alcohol or gel-forming fiber intake between the baseline and canola oil diets. There was a small difference in protein (2.7% en) and cholesterol (84 mg/d) between these two diets. The fatty acid distribution of the baseline diet for the canola group was SFA = 17.4% en, MUFA = 12.2% en and PUFA = 5.6% en. Analogous data for the canola intervention period were 14.0%, 15.1% and 8.1% en, respectively. The substitution of canola oil for butter on bread resulted in a significant ($p<0.01$) decrease in serum T-C (-7.8%) after three weeks, but this change was no longer significant after six weeks of feeding (-3.0%). Serum LDL-C decreased significantly ($p<0.001$) after three (-13.4%) and six weeks of feeding (-6.3%, $p<0.05$). There were no significant differences in serum HDL-C between these diets. The serum lipids of subjects given the control

diet did not change significantly, but the results were not compared statistically to the experimental diets. The theoretical effect per the Hegsted equations on serum T-C due to the small difference in dietary cholesterol between the baseline and experimental periods was 0.019 mmol/l compared to the observed change of 0.49 mmol/l at three weeks. Analogous data for serum LDL-C were 0.012 mmol/l compared to an overall change of 0.59 mmol/l. The small effects due to cholesterol do not detract materially from the beneficial effect of canola oil. There were no changes in body weight during the experiment. This study provides strong, credible evidence that a canola oil-water emulsion has a favorable effect on serum lipids when substituted for butter in the diet of middle-aged men and women. The results are particularly impressive given the relatively modest changes between the baseline and experimental diets. **[FDA quality rating +].**

Truswell *et.al.* (1992, 2000) conducted two series of experiments (one in 1990 and another in 1991) that examined the effect of feeding potato crisps containing either canola oil or palmolein on serum lipids in normocholesterolemic men and women. A randomized, double-blind cross-over design was used for both experiments with a three-week intervention period in the 1990 study and a five-week treatment period in the 1991 study. Male subjects consumed 53 g/d of the test fats and female participants consumed 35 g/d. The composition of the experimental diets was not provided, however, the fatty acid distribution (in percent by weight) of the canola oil was 16:0 = 5%; 18:0 = 3%; 18:1 = 63%; 18:2 = 20% and 18:3 = 8%. Analogous data for palmolein were 14:0 = 1%; 16:0 = 39%; 18:0 = 5%; 18:1 = 45%; 18:2 = 11% and 18:3 = 0%. Canola oil lowered serum T-C compared to palmolein by 10.5% in 1990 and by 6.2% in 1991 while having no effect on serum LDL-C concentrations. There was also a suggestion that canola oil decreased blood HDL-C compared to palmolein in the 1990 experiment but not in the one conducted in 1991. This

study was very difficult to interpret because dietary information was lacking, statistical analysis was incomplete and the canola oil used in the 1991 experiment was contaminated with palmolein. These shortcomings limit the conclusions that can be drawn from the study. **[FDA quality rating -]**

Valsta *et.al.* (1992) investigated the effect of diets high in canola oil, sunflower oil or SFAs on serum lipids by using a randomized, double-blind, cross-over design. Fifty-nine healthy (mean baseline serum T-C = 5.03 mmol/l) subjects (30 female) aged 18 to 65 years participated in the study. The baseline diet was fed for two weeks and subjects were randomized to one of the experimental diets for 25 days. The subjects were then crossed over to the other diet without a washout period. All three diets were similar in energy content, total fat (~37% en), cholesterol, protein, CHOs, dietary fiber and alcohol. The fatty acid content of the high-SFA baseline diet was 18.9% en SFAs, 11.0 % en MUFAs and 3.7% en PUFAs. Similar data for the canola oil diet were 12.4%, 16.2% and 7.6% en, respectively. Serum T-C decreased ($p<0.001$) by 15% after the canola oil diet compared to the baseline diet, and serum LDL-C fell by 6% ($p<0.01$). There was no change in serum HDL-C. There were no differences between the canola and sunflower oil diets in serum T-C or HDL-C, but the canola oil diet lowered serum LDL-C more ($p<0.01$) than the one with sunflower oil. Dietary intake was adjusted during the course of the experiment to maintain constant body weight. This study provides strong, credible evidence that canola oil has favorable effects on serum lipids compared to a diet higher in SFAs. **[FDA quality rating +]**

Nydalh *et.al.* (1993) studied the effect on serum lipids of substituting canola or sunflower oil for habitual fat sources among 101 (64 female) normocholesterolemic (mean baseline serum T-C =

4.79) students and teachers with a mean age of 29.2 years. The subjects consumed their habitual diet for four weeks and were then randomized to one of the test diets for a three-week treatment period. The subjects were crossed over to the other treatment for a similar period of time after a three-week washout interval during which the habitual diet was consumed. The paper did not provide the nutritional composition of the habitual diets, but indicated that most subjects consumed a typical Swedish diet. However, 22 subjects consumed various restricted (e.g., vegetarian) baseline diets. The canola oil diet resulted in a significant ($p<0.001$) reduction in serum T-C (-4%) and LDL-C (-5%, $p<0.01$) with no significant change in serum HDL-C (+2%). There were no significant changes in body weight during the course of the experiment. This paper provides suggestive evidence that canola oil has beneficial effects on serum lipids or normocholesterolemic individuals when substituted for other lipid sources in traditional Swedish diets, but the lack of dietary information limits the conclusions that can be drawn with respect to SFAs. **[FDA quality rating -]**

Seppänen-Laakso *et.al.* (1993) studied the effect of substituting canola or olive oil (as oil-water emulsions) for butter or margarine used as spreads on serum lipids. Fifty-seven (27 female) moderately hypercholesterolemic (serum T-C = 5.0 – 8.5 mmol/l), middle-aged (41.7 – 45.5 years) subjects participated in the study. They consumed their habitual diets before being randomized alphabetically to canola oil (n=23), olive oil (n=23) or control (n=11) groups. The control group continued to consume habitual diets, which consisted of subjects who used both butter and margarines. This parallel design experiment used a six-week intervention period. Canola oil intake was 17 g/d (15% en) and olive oil intake was 19 g/d (18% en) during this period. There were no significant differences between the baseline and canola oil diets in energy, total fat, SFAs,

MUFAs, cholesterol, protein, CHO, alcohol or gel-forming fiber content. There were no significant changes in serum T-C or LDL-C in the canola oil group at six weeks compared to baseline. HDL-C in this group was significantly increased at three (+5.7%, $p<0.01$), but not at six weeks (3.0%, NS) compared to baseline, however, the HDL-C/T-C ratio was significantly higher both at three (9.7%, $p<0.001$) and six weeks (7.1%, $p<0.01$). LDL-C was significantly reduced on the olive oil diet at three weeks (-7.5%, $p<0.01$), but not at six weeks compared to baseline. There was no change in HDL-C in the olive oil diets compared to baseline. There were no significant changes in the control group during the experiment, but results were not statistically compared to the intervention groups. Body weight remained constant throughout the experiment. These data suggest that replacing the habitual spreads used on bread with canola or olive oil can affect serum lipids. However, the composition of the experimental and baseline diets was quite similar (there was no statistical difference in SFA intake), so the effects were subtle. This observation is probably explained by the fact that both butter and margarines were consumed as components of the habitual diet. A statistical comparison between the effects of canola and olive oils was not provided. This study suggests that canola oil can have a positive impact on serum lipids when added to the diet, but the effect cannot be attributed to substitution for SFAs since this dietary constituent did not change during the course of the experiment. **[FDA quality rating Ø]**

Gustafsson *et.al.* (1994) used a randomized, parallel design to study the effect on serum lipids of adding canola or sunflower oil to a high-SFA baseline diet for three weeks. Ninety-five middle-aged (~46 years) subjects (22 female) with moderate hypercholesterolemia (baseline serum T-C = 6.5 – 9.0 mmol/l) participated in the study. The test fats were incorporated into the diets as oils, spreads and liquid margarine for cooking. There were no significant differences between the

experimental diets in energy, total fat (30% en), cholesterol, protein, CHO, dietary fiber or alcohol. However, the baseline diet differed from the experimental diets in energy, total fat (37.4 vs. 30% en), cholesterol, CHO, dietary fiber and alcohol. The fatty acid content of the baseline diet was SFAs = 16.0% en, MUFAs = 13.0% en and PUFAs = 5.7% en. Analogous data for the canola oil diet was 7.2%, 14% and 6.5% en, respectively. There was a significant decrease in serum T-C (-15%, $p<0.001$), LDL-C (-16%, $p<0.001$) and HDL-C (-11%, $p<0.05$) on the canola oil diet compared to baseline. The decrease in HDL-C on this diet was smaller than that of LDL-C so the change in the LDL/HDL ratio (-6%, $p<0.05$) was beneficial. There were no significant differences between the two test oils in any of the serum lipid parameters. Body weight decreased by 1% during the study in both experimental groups. This study was designed primarily to examine the difference between canola and sunflower oils. Differences in the composition of the baseline and experimental diets make it difficult to isolate the effect of canola oil as a replacement for SFAs in this experiment. Nevertheless, this study provides additional evidence that canola oil has favorable effects on serum lipids compared to diets higher in SFA. **[FDA quality rating Ø]**

Miettinen and Vanhanen (1994) studied the effect of adding squalene to a canola oil diet among 18 moderately hypercholesterolemic (mean baseline serum T-C = 7.1 mmol/l) male subjects with a mean age of 50 years. The experiment used a four-phase parallel design. Fifty grams of canola oil was provided to all subjects as a replacement for 50 g of habitual dietary fat prior to randomization into one of four groups containing different amounts of squalene. Detailed dietary information was not provided, but the fatty acid content of the diet after addition of canola oil was 10.5% en as SFAs, 19.5% as MUFAs and 3.4% as PUFAs. The intake of animal fat and cholesterol was

"reduced" after adding canola oil. Detailed lipid data were not provided, however the replacement of habitual dietary fat with canola oil resulted in a significant ($p<0.05$) decrease in serum T-C (-9%), LDL-C (-10%) and increase in HDL-C (9%). Body weights did not change during the experiment. This study has limited applicability to the proposed claim because detailed dietary data were not provided. Nevertheless, the results provide additional evidence that canola oil has positive effects on serum lipids when substituted for more saturated dietary fats. **[FDA quality rating -]**

Uusitupa *et.al.* (1994) compared the effect of a high SFA-containing diet and a diet enriched with low-erucic acid rapeseed (canola) oil on serum lipids among 10 normocholesterolemic (mean baseline serum T-C = 5.21 mmol/l) young (mean age = 23 years) females. The subjects were randomized to one of the experimental diets for three weeks before being changed to the opposite diet after a two-week washout period. A low-fat (24.8% en) habitual diet was consumed before randomization and during the washout periods. The primary source of fat in the SFA diet was butter and the test fats were provided as spreads, vegetable oils and various dairy products. There was no difference between the experimental diets in energy, total fat (~39% en), protein, CHO, or dietary fiber. The habitual and SFA diets contained more cholesterol than the canola oil diet (~181 and 213 mg/d vs. 107mg/d, respectively), but all diets were low in this constituent. Serum T-C decreased significantly after the canola oil diet compared to the SFA diet (-21.6%, $p<0.001$). Serum LDL-C was also significantly reduced (-29%, $p<0.001$). These diets had no effect on serum HDL-C. The small difference in dietary cholesterol between these two diets (13.5 mg/MJ) is unlikely to have materially affected the results. The theoretical change in serum T-C (calculated as above according to Hegsted *et.al.*, 1993) was 0.098 mmol/l, which is much less than the difference

observed in this parameter between the two diets (1.16 mmol/l). Similarly, the theoretical change in serum LDL-C due to this difference in dietary cholesterol was only 0.06 mmol/l compared to the observed change of 0.99 mmol/l. Serum T-C (-18%, $p<0.01$) and LDL-C (-26.6%, $p<0.01$) also decreased in the canola oil diet compared to the habitual (baseline) diet, but there was no significant change in HDL-C. Body weights decreased slightly (0.9 kg) during the study in both experimental groups. The authors concluded that these small changes were unlikely to have significantly affected the results. This study provides good evidence that canola oil reduces serum T-C and LDL-C when compared to diets higher in SFAs. **[FDA quality rating Ø]**

Sundram *et.al.* (1995) studied the effect on serum lipids of a low-fat baseline diet, an AHA Step 1 diet, a canola oil-containing diet and a diet high in palmolein by using a randomized, cross-over design. Twenty-three young (10-24 years), normocholesterolemic (mean baseline serum T-C = 174 mg/dl) male subjects who were members of the Malaysian military participated in the study. The subjects were randomized to one of the test diets for four weeks after consuming the baseline diet for three weeks. There were no significant differences among the baseline, Step 1 or experimental diets in energy content, total fat (~30% en), cholesterol, protein or CHO. The test oils comprised approximately 20% of total energy. The fatty acid content of the baseline, Step 1, canola and palmolein diets were 12.2%, 10.1%, 6% and 13% en, respectively. Analogous data for MUFAs were 12%, 12.9%, 17.5% and 14.3%, while those for PUFAs were 3.8%, 8.3%, 7.7% and 4.1% en. The palmolein diet had more ($p<0.05$) palmitic acid (11.2% en) than the canola (3.9% en) or Step 1 (8.2% en) diets. There was no difference in serum T-C or LDL-C between the experimental diets. Serum HDL-C decreased by 14.6% in both the canola and palmolein group compared to the Step 1 group. The difference between these values for the Step 1 and canola oil

diet was significant ($p<0.01$) by repeated measures analysis of variance (ANOVA), but the change was not significant according to the paired t-test. The difference in HDL-C between the palmolein and Step 1 diets was not statistically significant. Body weights did not change during the experiment. This study does not support the hypothesis that canola oil reduces serum T-C and LDL-C when compared to a diet higher in SFAs. However, the unique fatty acid distribution of palmolein may partially explain this observation. Palmitic acid located in the 2-position of the triglyceride has been shown to be more hypercholesterolemic than the same fatty acid found in the 1- or 3-positions (Elson, 1992). Kritchevsky *et.al.* (2002) demonstrated that native palm oil (which has only 2.58 of its palmitic acid in the 2-position) is less hypercholesterolemic than randomized palm oil with 13.6% of its palmitic acid in this position. Therefore, native palm oil may be less hypercholesterolemic than its SFA content would predict. In addition, the fact that the participants were normocholesterolemic makes it more difficult to obtain a hypocholesterolemic response. Furthermore, the subjects in this study were very lean (BMI = 21.3) and accustomed to a low-fat Malaysian diet. These factors limit the applicability of this study to the general U.S. population. **[FDA quality rating +]**

Valsta *et.al.* (1995) conducted a randomized, double-blind cross-over study to compare the effect on serum lipids of diets rich in canola and sunflower oils to that of a habitual diet. Forty (20 female), normocholesterolemic (mean baseline serum T-C = 4.66 mmol/l) subjects aged 20 to 46 years participated in the study. The habitual diet was monitored for six weeks before randomization and was provided during a six-week washout period between treatments. The intervention periods were also six weeks in duration. The test fats were provided as special margarines, salad dressings, food oils and specially prepared baked goods. There were no

significant differences between the canola and sunflower oil diets in energy, total fat, SFAs, MUFAs, PUFAs, cholesterol, protein or alcohol. A statistical comparison between the experimental and baseline diets was not provided, but the latter appeared to be lower in total fat (33% vs. 40.8% en), MUFAs (11.2% vs. 17.8% en), PUFAs (5.1% vs. 8.5% en) and higher in cholesterol (348 vs. 270 mg/d) and SFAs (13.9 vs. 11.2% en) compared to the canola oil diet. The latter resulted in lower serum T-C (-9.4%, $p<0.01$) and LDL-C (-22%, $p<0.01$) than the baseline diet, but there was no change in serum HDL-C. There was also no change in serum T-C (-8.5%, NSD) or HDL-C on the sunflower oil diet compared to baseline, but LDL-C decreased (-21%, $p<0.01$). Body weight was held constant during the study by adjusting the energy content of the diets. This study was designed primarily to compare the effects of canola and sunflower oils. Therefore, the baseline diet was not adjusted to have similar macronutrient contents as the experimental diets. For that reason, it is not possible to conclude that the changes observed in serum lipids compared to the baseline are due exclusively to differences in fatty acid intake. Nevertheless, this study provides additional evidence that canola oil has favorable effects on serum lipids compared to a diet higher in SFAs. **[FDA quality rating Ø]**

Matheson *et.al.* (1996) studied the effect of a high canola oil diet compared to a habitual diet (higher in SFAs) on serum lipids among 23 (one female) members of an Antarctic expedition aged 25 to 50 years. The participants were mildly hypercholesterolemic (mean baseline serum T-C = 5.82 mmol/l). The study used a non-randomized, cross-over protocol in which the habitual diet was consumed for 15 weeks followed by a canola oil diet for 12 weeks. The subjects then returned to the habitual diet for an additional 12 weeks. The baseline diet was similar ($p>0.05$) to the canola oil diet at the end of the 12-week intervention period in energy, total fat (~37.5% en),

cholesterol, protein, CHO and dietary fiber. The SFA content of the baseline and experimental diets was 15.9% and 13.3% en, respectively. Analogous data for MUFAs and PUFAs were 13.4% vs. 16.2% and 6% vs. 5.3% en, respectively. The canola oil diet lowered serum T-C by 7.0% ($p<0.016$) and LDL-C by 10.0% ($p<0.016$) compared to the habitual diet. Serum HDL-C values increased slightly (5.6%, NSD). Body weight increased slightly (0.8 kg) during the course of this 42-week experiment. It seems unlikely that this small weight gain materially impacted the results. However, any effect of weight gain that occurred would have detracted from, not augmented, the canola oil response. This study provides additional evidence that canola oil has favorable effects on serum lipids compared to a diet higher in SFAs. **[FDA quality rating Ø]**

Jenkins *et.al.* (1997) conducted two randomized, placebo-controlled, cross-over studies to examine the effect of adding psyllium to diets with two different MUFA contents. The intervention periods were one month, and there was a six-week washout period during which an AHA Step 2 diet was provided. The Step 2 diet also served as the baseline for all treatments. The first experiment utilized 32 (17 female) moderately hypercholesterolemic (mean baseline serum T-C = 7.06 mmol/l) subjects (mean age = 57.5) and the second experiment included 27 participants with similar T-C values and ages. Experiment 1 employed a 6% MUFA-containing diet with or without 1.4 g psyllium per MJ. Experiment 2 utilized similar diets to which canola oil had been added to increase the MUFA content to 12% en. Therefore, it is possible to isolate the effect of adding canola oil to these diets by comparing the 6% and 12% MUFA-containing diets (both with and without added psyllium). There were no differences between the 6% and 12% MUFA-containing diets in protein or ethanol content, but the 12% MUFA diets had slightly more energy, substantially more total fat (72 vs. 46 g/d) and less cholesterol (22 vs. ~30 mg/d) than the 6%

MUFA diets. The fatty acid content of the 6% MUFA diets (both control and psyllium) was: SFA = 11 g/d; MUFA = 15 g/d and PUFA = 19-20 g/d. Similar data for the 12% MUFA diets were: SFA = 15 g/d; MUFA = 30-31 g/d and PUFA = 25 g/d. The change in serum lipids for each of these diets was compared to the baseline (Step 1) diet. With respect to the control (non-psyllium) diets, the changes in serum lipids for the 6% and 12% MUFA diets were: serum T-C (-4.9% and -10.2%, respectively); serum LDL-C (-4.3% and -7.4%, respectively); and HDL-C (-3.4% and -1.6%, respectively). Analogous data for the psyllium-containing diets at 6% and 12% MUFA were: serum T-C (-9.7% and -12.2%, respectively); serum LDL-C (-12.3% and -15.3%, respectively); and HDL-C (-10.9% and -8.1%, respectively). These data show that there was a greater reduction in T-C and LDL-C and less reduction in HDL-C for the higher MUFA diets compared to their lower MUFA counterparts at both levels of psyllium, however, statistics for these comparisons were not provided. Nevertheless, the paper noted that there was a significant ($p=0.035$) negative correlation ($r = -0.31$) between percent of energy from MUFAs and serum T-C using combined control and psyllium data. A similar result was also seen for the ratio of T-C to HDL-C ($r = -0.44$; $p=0.002$). There were no changes in body weight during this study. Although it was designed primarily to examine the effect of psyllium on serum lipids at different levels of dietary MUFAs, this study provides additional evidence that canola oil has positive effects on serum lipids compared to diets higher in SFAs. However, the difference in the macronutrient content between the 6% and 12% MUFA diets makes it difficult to attribute this effect to canola oil *per se*. **[FDA quality rating Ø]**

Noakes and Clifton (1998) investigated the effect of canola oil and high-SFA diets on serum lipids among 18 (six female) moderately hypercholesterolemic (mean baseline serum T-C ~6.5 mmol/l)

subjects (mean ~53 years). The subjects consumed a low-fat (<25% en) diet for two weeks and were then randomized to a butter-containing diet high in SFAs, a canola oil diet or a partially hydrogenated canola oil diet for three-week treatments using a cross-over design. The paper did not indicate whether a washout period was used between treatments. (The study included a separate experiment of similar design using partially hydrogenated and non-hydrogenated PUFAs, but these results will not be discussed because they are not germane to the proposed claim.) There were no significant differences between the butter and unhydrogenated canola oil diets with respect to energy, total fat (~31% en), protein, CHO, dietary fiber or alcohol. The cholesterol content of the butter diet (298 mg/d) was higher ($p<0.01$) than the unhydrogenated canola oil diet (195 mg/d). The butter diet provided 15.5% en as SFAs, 10.1% en as MUFAs and 2.8% en as PUFAs. Analogous data for the canola diet were 8.7%, 14.5% and 6.0% en, respectively. There were numerous differences in macronutrient content between the baseline and canola oil diets. The latter resulted in significant ($p<0.01$) decreases in T-C (-8.4%), LDL-C (-12.8%) and the T-C/HDL-C ratio (-13.5%) compared to the high SFA diet. There were no significant changes in HDL-C between these two diets. The theoretical effect (according to Hegested *et.al.*, 1993) of the difference in dietary cholesterol (34 mg/1,000 kcal) between the butter and canola oil diets on T-C (0.059 mmol/l) and LDL-C (0.39 mmol/l) accounted for only 11.5% and 7.4% of the difference, respectively, between these two diets. Therefore, it is likely that the effect of UFAs from canola oil was significant despite the difference in cholesterol intake. There were no changes in body weight during the experiment. This study provides strong, credible evidence that canola oil has a favorable effect on serum lipids compared to a diet higher in SFAs. **[FDA quality rating +]**

Sarkkinen *et.al.* (1998) used a randomized, single-blind, parallel design to study the effect of canola oil and three other diets on serum lipids among 160 (83 female) moderately hypercholesterolemic (mean baseline serum T-C ~6.5 mmol/l) subjects (mean age ~45 years). The subjects were randomized to one of the following four diets for six months after a two-week run-in period during which their habitual diet was consumed: a high-fat, high-SFA diet containing butter; a high-fat, high-MUFA diet containing canola oil (provided as a special margarine); a low-fat, high-PUFA diet containing sunflower oil (provided as a special margarine); or a low-fat diet containing a mixture of butter and canola oil. The control and canola oil diets appeared to have comparable contents of energy, total fat, protein, CHO, dietary fiber and alcohol, but statistical comparisons were not provided. The target for total fat was 38% en for both diets, but the actual results were 35% en for the control diet and 33.9% for the canola diet. The control diet had more cholesterol (301 mg/d) than the canola oil diet (230 mg/d). The fatty acid content (% en for SFAs, MUFAs and PUFAs) of the control diet was 14.5%, 10% and 3.6% en, respectively, and that of the canola oil diet was 10.6%, 11.3% and 5.4%. Serum LDL-C decreased by 6.5% ($p<0.01$ to 0.001) on the canola oil diet compared to the baseline but there were no changes in T-C or HDL-C. Furthermore, serum T-C was 3.5% lower and LDL-C was 3.0% lower on the canola oil diet compared to the control diet, but these differences were not statistically significant. Body weight did not change during the course of the experiment. This study provides only suggestive evidence that canola oil has beneficial effects on serum lipids compared to a diet higher in SFAs. The lack of a significant response to the canola diet compared to the control may have been due to the small difference in MUFAs (11.3% vs. 10.0% en, respectively) and PUFAs (5.4% vs. 3.6% en) between the two diets. **[FDA quality rating +]**

Hodson *et.al.* (2001) studied the effect on serum lipids of diets high in canola or safflower oil compared to a diet high in SFAs using a randomized, cross-over design with 2.5-week intervention periods. A washout phase between treatments was not used. This paper reported results for the MUFA and PUFA experiments as separate trials, but only the MUFA results are germane to the proposed claim. Forty-two (35 female), normo- to moderately hypercholesterolemic (mean baseline serum T-C <6.5 mmol/l), young (mean age = 23 years) subjects participated in the canola oil phase of the study. The SFA diet had more energy (9.9 vs. 8.2 MJ, $p<0.001$), total fat (34.0% vs. 28.9% en, $p<0.001$) and cholesterol (305 vs. 168 mg/d, $p<0.001$) than the canola oil diet and less CHOs (48.7 vs. 53.8% en, $p<0.0010$). There were no significant differences in protein, dietary fiber or alcohol contents. The SFA diet contained 17.7% en SFAs, 9.7% en MUFAs and 3% PUFAs while the canola oil diet contained 8.4% en SFAs, 11.6% en MUFAs and 6.1% PUFAs. Serum T-C was 12% lower ($p<0.001$), LDL-C 15% lower ($p<0.001$) and HDL-C 4% lower ($p<0.05$) after the canola oil diet than after the SFA diet. Body weights did not change during the course of the experiment. This study provides additional evidence that canola oil has favorable effects on serum lipids compared to diets higher in SFAs, but multiple differences in the composition of the experimental diets makes it difficult to assign the effect to canola oil *per se.* **[FDA quality rating Ø]**

Gulesserian and Wildhalm (2002) studied the effect of substituting canola oil for more highly saturated sources of dietary fat on serum lipids among 17 (11 female) children and adolescents with a family history of hypercholesterolemia. This experiment was a non-randomized feeding study in which subjects were instructed to consume a low-fat diet that included 15 g of canola oil during the first two months and 22 g/d during the following three months. No information was

provided on the nutritional composition of the baseline diet. The intervention diet contained 29.5% en total fat with a fatty acid distribution of 39% by weight SFAs, 30% MUFAs and 21% PUFAs. The dietary intervention resulted in a 9% decrease in serum T-C ($p<0.05$), a 6% decrease in LDL-C ($p<0.007$) and a non-significant decrease in HDL-C. Body weight distribution (based on weight and length) did not change during the study. This research provides suggestive evidence that canola oil has a favorable effect on serum lipids in children and adolescents compared to a higher fat and SFA-containing diet, but a lack of dietary and other information limits the conclusions that can be drawn. **[FDA quality rating -]**

Karvonen *et.al.* (2002) studied the effect on serum lipids of replacing ordinary cheese and cold cuts with canola oil-based cheese in the diets of 31 (14 female) moderately hypercholesterolemic (mean baseline serum T-C = 6.13 mmol/l) subjects (mean age = 52.9 years). The study used a single-blind, randomized, cross-over design with a two-week run-in period and four-week treatments. There were no differences between the experimental diets in energy, cholesterol, CHOs or dietary fiber. The canola diet had slightly less total fat (31.1% vs. 32.7% en, $p=0.041$) and slightly more protein (18.5% vs. 17.2% en, $p=0.01$), but the physiological significance of these differences is probably small. The canola diet contained 9.6% en SFAs, 12% en MUFAs and 6.4% PUFAs while the high-SFA diet provided 14.1% en SFAs, 10.4% en MUFAs and 4.7% PUFAs. Mean serum T-C was 5% lower ($p<0.001$) and LDL-C was 6.4% lower ($p=0.002$) at the end of the canola-containing diets than after the control cheese diets. There were no differences in serum HDL-C after these diets. Body weights did not change during the course of the experiment. This study provides strong evidence that substituting canola oil-containing foods for foods higher in SFAs promotes favorable changes in serum lipids. **[FDA quality rating +]**

The effect on serum lipids of diets rich in canola, olive or sunflower oil compared to a baseline diet high in SFAs was studied by Kratz *et.al.* (2002). The experiment used a randomized, parallel design with an intervention period of four weeks. Fifty-eight (27 female), normocholesterolemic (mean baseline serum T-C = 4.89 mmol/l) subjects (mean age = 26 years) consumed a high-fat/high-SFA run-in diet for two weeks and were then randomized to one of the three experimental diets. The wash-in and experimental oil diets appeared to be similar in energy and all macronutrients and cholesterol, but comparative statistics were not provided. The total fat content of all diets was 38% en. The SFA content of the wash-in, canola oil, olive oil and sunflower oil diets was 19.1%, 9.1%, 10.7% and 1% en, respectively. Analogous data for MUFAs were 11.3%, 19.1%, 23.3% and 8.7% en, respectively, and those for PUFAs were 5.6%, 9%, 3.4% and 18.5% en, respectively. Serum T-C, LDL-C and HDL-C all fell significantly on the canola oil diet compared to the diet high in SFAs (-14.3%, $p<0.001$; -17.5%, $p<0.001$; and -12.6%, $p<0.01$, respectively). Analogous data for the olive oil diet were -9.2%, $p<0.001$; -10.7%, $p<0.01$ and -8.0%, $p<0.01$ and those for the sunflower oil diet were -16.7%, $p<0.001$; -19.7%, $p<0.001$ and -12.5%, $p<0.001$. Body weight did not change during the course of the experiment. This study provides strong, credible evidence that dietary canola oil lowers T-C and LDL-C compared to diets higher in SFAs. **[FDA quality rating +]**

b. Studies that compare canola and olive oil-containing diets

FDA has already permitted a QHC regarding consumption of MUFAs from olive oil and CHD. Therefore, relevant studies that compared canola oil-containing diets to olive oil-containing diets are summarized below to provide credible evidence that canola oil is at least as beneficial as olive oil in its effects on serum lipids.

Lichtenstein *et.al.* (1993) compared the effect on serum lipids of canola, olive and corn oils when incorporated into a Step 2 diet. These data were also published by Jones *et.al.* (1994) and by Lichtenstein *et.al.* (1994). Fifteen (8 female) subjects aged 44 to 78 years consumed a typical American diet (35% en total fat, 12.9% en SFAs, 12.2% MUFAs, 7.9% PUFAs and ~350 mg/d cholesterol) for 32 days and were then randomized to one of the test oils for 32 days. After that, subjects were switched to each of the other diets for a similar period of time, according to a randomized, cross-over design. There was a two-week washout period between treatments during which the baseline diet was consumed. The subjects were selected to be moderately hypercholesterolemic (mean baseline serum T-C = 234 mg/dl). The test diets were similar in all macronutrients (total fat ~30% en) and cholesterol. The test fats comprised approximately two-thirds of total dietary fat. The canola oil diet provided 5.4% en SFAs, 14.5% en MUFAs and 6.7% en PUFAs and the olive oil diet contained 6.9% en SFAs, 17% en MUFAs and 3.9% en PUFAs. Serum T-C was significantly lower ($p<0.01$) at the end of the treatment period for canola oil (194 mg/dl) compared to olive oil (205 mg/dl). Serum LDL-C (126 mg/dl for canola oil and 132 mg/d for olive oil) and HDL-C (44 and 46 mg/dl, respectively) were similar ($p>0.05$) for both diets. The diets lowered all three serum lipid classes with respect to the baseline, but the change in HDL-C for olive oil was not statistically significant as it was for the other two fats. There were no significant weight changes during the course of the experiment. This study provides strong evidence that canola oil is as good as or better than olive oil in beneficially affecting serum lipids. The study also suggests that canola oil lowers serum T-C and LDL-C with respect to diets higher in SFAs, but differences in the macronutrient content of the baseline and experimental diets makes it difficult to attribute the effect to canola oil *per se.* **[FDA quality rating +]**

Nydahl *et.al.* (1995) studied the effect on serum lipids of substituting canola or olive oil for habitual fat sources in the typical Swedish diet among 22 (10 female) hypercholesterolemic (mean baseline T-C = 307 mg/dl) subjects with a mean age of 54.2 years. A randomized, cross-over protocol with 3.5-week intervention periods was used. There was no washout interval between treatments. The nutritional composition of the habitual diet was not provided, but the paper stated that it was assumed to be higher in fat than the experimental diets. The latter were virtually identical in all macronutrients and cholesterol. Total fat content was 30% en. The fatty acid content of the canola oil diet was 8% en SFAs, 13% en MUFAs and 7% en PUFAs and that of the olive oil diet was 8% en SFAs, 15% en MUFAs and 5% en PUFAs. Serum T-C for the canola and olive oil diets decreased ($p<0.001$) compared to baseline by 17% and 14%, respectively, while LDL-C fell ($p<0.001$) by 20% and 16%, respectively. There were no significant changes in serum HDL-C. Body weights remained constant throughout the experiment. This study shows that canola oil is as good as olive oil in affecting favorable changes in serum lipids among hypercholesterolemic individuals. The applicability of these data to the proposed claim is somewhat limited because FDA has concluded that hypercholesterolemic subjects do not reflect the normal, healthy U.S. population for the purpose of substantiating health claims. Nevertheless, the subjects in this experiment were barely above FDA's benchmark of 300 mg/dl, and it is likely that similar results would have been obtained had their T-C concentrations been slightly lower (e.g., 290 mg/dl). In any case, the results are a valid comparison of the two oils for this population. **[FDA quality rating +]**

A study by Kratz *et.al.* (2002) discussed in the previous section of this document provided data on the effect of canola oil on serum lipids as both a replacement for dietary SFAs and in comparison to olive and sunflower oils. As noted in the previous discussion, this study showed that all three

oils lowered T-C and LDL-C compared to diets higher in SFAs among 58 (27 female), normocholesterolemic (mean baseline serum T-C = 4.89 mmol/l) subjects (mean age = 26 years). Serum T-C, LDL-C and HDL-C all fell significantly on the canola oil diet compared to the one high in SFAs (-14.3%, $p<0.001$; -17.5%, $p<0.001$; and -12.6%, $p<0.01$, respectively). Analogous data for the olive oil diet were -9.2%, $p<0.001$; -10.7%, $p<0.01$ and -8.0%, $p<0.01$ and those for the sunflower oil diet were -16.7%, $p<0.001$; -19.7%, $p<0.001$ and -12.5%, $p<0.001$. These data show that there was no significant difference ($p>0.05$) between the effect of canola and olive oils on serum T-C or LDL-C. Olive oil lowered serum HDL-C significantly ($p<0.05$) less than the canola or sunflower oil diets, but the ratio of T-C to HDL-C for canola and olive oils was virtually identical. This study showed that canola and olive oils had equivalent effects on serum lipids under the conditions of this experiment. **[FDA quality rating +]**

A randomized, double-blind, cross-over design with three-week treatment periods was used by Pedersen *et.al.* (2000) to study the effects of canola, olive and sunflower oils on serum lipids among 18 normocholesterolemic (mean baseline serum T-C = 4.74 mmol/l) male students aged 20 to 28 years. Subjects consumed their habitual diet before the study and during 5- to 12-week washout periods between treatments. All food was prepared for the subjects and no additional food was permitted. The three test diets were virtually identical in total fat (35% en), cholesterol, protein, CHO and dietary fiber. The canola oil diet provided 9% en as SFAs, 18% en as MUFAs and 7% en as PUFAs. Analogous data for the olive oil diet were 11%, 21% and 3%, en, respectively, and those for the sunflower oil diet were 10%, 9%, and 15% en, respectively. There were no significant differences for serum T-C or HDL-C between the canola and olive oil diets at the end of their respective treatment periods. However, serum LDL after the canola oil treatment

(1.73 mmol/l) was significantly ($p<0.001$) lower than after olive oil feeding (2.16 mmol/l). The ratios of LDL to HDL, and of T-C to HDL were also significantly ($p<0.01$) lower after the canola oil diet compared to the olive oil diet. There were no significant changes in body weight during the experiment. This study provides strong, credible evidence that canola oil is as good as or better than olive oil in beneficially affecting on serum lipids in young, normocholesterolemic male subjects. **[FDA quality rating +]**

Nielsen *et.al.* (2002) studied the effect of diets rich in canola, olive or sunflower oil on serum lipids among 18 normocholesterolemic (mean baseline serum T-C = 2.46 – 6.01 mmol/l) males with a mean age of 23.9 years. All subjects consumed their habitual diets before the study and were then randomized to one of the experimental diets for three weeks. A double-blind cross-over protocol was employed so that all participants consumed each diet separated by 4 to 12-week washout periods during which habitual diets were consumed. All diets were provided and strictly controlled. The diets were similar in all macronutrients and cholesterol and provided 32-33% en as total fat. The fatty acid distribution (expressed as percent of total fatty acids) of the canola oil diet was 28.7% SFAs, 49.5% MUFAs and 21.8% PUFAs. Analogous data for the olive oil diet were 33.5% SFAs, 58.3% MUFAs and 8.2% PUFAs. The canola oil diet compared to the olive oil diet resulted in lower fasting blood T-C (3.5 vs. 4.1 mmol/l, $p<0.001$) and LDL-C values (2.7 vs. 2.2, $p<0.001$). There were no differences in fasting HDL-C concentrations. These data provide strong, credible evidence that canola oil is as good as or better than olive oil in favorably affecting serum lipids. **[FDA quality rating +]**

c. Canola oil studies not applicable to the proposed claim

The following CHD-related canola oil studies will not be discussed because they are not applicable to the proposed claim for the following reasons: serum T-C and/or LDL-C data were not provided (Mutanen *et.al.*, 1992; Freese *et.al.*, 1994; Turpeinen *et.al.*, 1995; Valsta *et.al.*, 1996; Berglund *et.al.*, 1999; Kratz *et.al.*, 2002a; Lind *et.al.*, 2002; Kratz *et.al.*, 2003), canola oil diets were not compared to SFAs or olive oil (Chan *et.al.*, 1991), no significant difference in fatty acid intake occurred between the canola oil and comparative diets (Sinclair *et.al.*, 1999), subjects had a history of CHD (Herrmann *et.al.*, 1995; de Lorgeril *et.al.*1999[13]), insufficient dietary data (Sylling *et.al.*, 1999), were unable to assess the effect of canola oil due to mixed dietary sources of UFAs and/or used multiple interventions (Howard *et.al.*, 1995; Becker *et.al.*, 1999; Luscombe *et.al.*, 1999; Metcalf *et.al.*, 2003; Müller *et.al.*, 2003; Smith *et.al.*, 2003). Nevertheless, copies of these papers are appended to this document in order to provide FDA with the totality of available evidence in the area of the proposed claim.

3. Summary of scientific publications on UFAs from canola oil and CHD

In summary, the weight of the available evidence shows that canola oil has favorable effects on serum lipids. The 21 studies discussed in this section that compare canola oil-containing diets with those higher in SFAs are enumerated in Table 3 along with their FDA quality ratings and levels of support for the proposed claim. Seven of the nine highest quality studies provide strong support for this claim and 11 of 12 lower quality studies provide suggestive support. Only three studies fail to show that canola oil lowers serum T-C and/or LDL-C when substituted for dietary SFAs. Two of these studies (Seppänen-Laakso *et.al.*, 1993; Sarkkinen *et.al.*, 1998) fed subjects relatively

[13] This paper is the final report of the Lyon Diet Heart Study. Numerous other publications regarding this study have been published, but the separate references are not enumerated in this petition for the sake of conciseness.

small amounts of canola oil, so that differences between the control and experimental diets with respect to SFAs and UFAs may not have been sufficient to elicit a significant response. The third study (Sundram *et.al.*, 1994) used normocholesterolemic, Malaysian subjects who consumed a characteristically low-fat (29% en) baseline diet and one of three experimental diets that were also low in total fat (31.3-31.8% en). In addition, the subjects were very lean (mean BMI = 21.3), exceptionally fit members of the military. These factors limit the applicability of this study to the normal U.S. population. Furthermore, this study used palm oil, which may be less hypercholesterolemic than other lipids with similar SFA content due to the location of palmitic acid on the triglyceride (Kritchevsly *et.al.*, 2002).

Table 3
Levels of Support for Proposed Claim by Individual Studies for Each FDA Quality Rating

FDA Quality Rating		
+	Ø	-
Baudet *et.al.* (1988)*	*McDonald et.al. (1989)*	*Truswell et.al. (1992)*
Wardlaw *et.al.* (1991)	Seppänen-Laakso *et.al.* (1993)	*Nydahl et.al. (1993)*
Seppänen-Laakso *et.al.* (1992)	*Gustafsson et.al. (1994)*	*Miettinen & Vanhanen (1994)*
Valsta *et.al.* (1992)	*Uusitupa et.al. (1994)*	*Gulesserian & Wildhalm (2002)*
Sundram *et.al.* (1995)	*Valsta et.al. (1995)*	
Noakes and Clifton (1998)	*Matheson et.al. (1996)*	
Sarkkinen *et.al.* (1998)	*Jenkins et.al. (1997)*	
Karvonen *et.al.* (2002)	*Hodson et.al. (2001)*	
Kratz *et.al.* (2002)		

*Studies in **bold** provide strong, credible support for the proposed claim. Studies in *italics* provide suggestive support and studies in plain type do not support the proposed claim.

Fifteen of the studies discussed above show that replacing sources of SFAs with canola oil results in a significant increase or no change in serum HDL-C. Five studies (McDonald *et.al.*, 1989; Gustafsson *et.al.*, 1994; Jenkins *et.al.*, 1997; Hodson *et.al.*, 2001; Kratz *et.al.*, 2002) reported a decrease in serum HDL-C among canola oil-fed subjects, but the decreases were less than those of serum T-C and LDL-C, so the overall effect on serum lipids was beneficial. Sundram *et.al.* (1995), who found no effect of canola oil feeding on serum T-C or LDL-C, reported a decrease in

serum HDL-C among subjects fed canola oil compared to palm oil. However, as noted above, the characteristics of the subjects and diets used in this study limit its applicability to the general U.S. population.

FDA identified studies it considered "most persuasive" in helping it to evaluate the QHC for olive oil[14]. Studies that allowed the agency to determine "whether there is a relationship between the substance and disease outcome" fell into this category. The characteristics of such studies include 1) the source of MUFAs used in the intervention group(s) could be attributed exclusively to olive oil; 2) the macronutrient content of the control and experimental groups were similar; 3) the intervention period was sufficient (at least three weeks) to ensure that changes in serum lipids were due to the dietary treatment; and 4) appropriate statistics were provided to compare the treatment and control diets.

Nine studies discussed in this section meet FDA's criteria for persuasiveness. Five studies (Valsta *et.al.*, 1992; Uusitupa *et.al.*, 1994; Matheson *et.al.*, 1996; Karvonen *et.al.* 2002; Kratz *et.al.* 2002) met all criteria, including control and experimental diets that were virtually identical in macronutrient and cholesterol content. Four additional studies (Baudet and Jacotot, 1988; Wardlaw *et.al.*, 1991; Seppänen-Laakso *et.al.*, 1992; Noakes and Clifton, 1998) also were deemed persuasive after determining that small differences in dietary cholesterol between the experimental and control groups did not materially impact serum T-C or LDL-C, according to established regression equations (Hegsted, 1993).

[14] http://www.cfsan.fda.gov/~dms/qhcolive.html .

Five additional studies showed that canola oil is at least as beneficial as olive oil with respect to serum lipids. Three studies (Lichtenstein *et.al.*, 1993; Pedersen *et.al.*, 2000; Nielsen *et.al.*, 2002) found that canola oil prompted a greater decrease in serum T-C and/or LDL-C than olive oil, while two studies (Nydahl *et.al.*, 1995; Kratz *et.al.*, 2002) found no difference.

In conclusion, the published intervention studies provide consistent, credible evidence that UFAs from canola oil lower serum T-C and/or LDL-C in healthy human subjects compared to diets higher in SFAs. In addition, these studies show that dietary UFAs from canola oil are as good as or better in this regard than diets containing olive oil.

D. Recommendations from governmental and professional organizations

Numerous public heath organizations have recommended that consumers choose diets low in SFAs and cholesterol while emphasizing UFAs as the predominant source of dietary fats. Many of these authoritative bodies specifically recommend canola oil as an aid in the management of CHD risk. Examples of these recommendations are presented below.

1. 2005 Dietary Guidelines for Americans

The Dietary Guidelines for Americans (U.S. Department of Agriculture, U.S. Department of Health and Human Services, 2005) recommend:

> To meet the total fat recommendation of 20 to 35 percent of calories, most dietary fats should come from sources of polyunsaturated and monounsaturated fatty acids. Sources of omega-6 polyunsaturated fatty acids are liquid vegetable oils, including soybean oil, corn oil, and safflower oil. Plant sources of omega-3 polyunsaturated fatty acids (α-linolenic acid) include soybean oil, **canola oil**, walnuts, and flaxseed… Plant sources that are rich in monounsaturated fatty acids include vegetable oils (e.g., **canola**, olive, high oleic safflower, and sunflower oils) that are liquid at room temperature and nuts. (emphasis supplied)

2. Healthy People 2010

Healthy People 2010 (U.S. Department of Health and Human Services, 2000) outlines specific health objectives for the nation. This document acknowledges that sources of UFAs, including canola oil, "can help lower health risks."

> The major vegetable sources of monounsaturated fatty acids include nuts, avocados, olive oil, **canola oil**, and high-oleic forms of safflower and sunflower seed oil. The major sources of polyunsaturated fatty acids are vegetable oils, including soybean oil, corn oil, and high-linoleic forms of safflower and sunflower seed oil and a few nuts, such as walnuts. Substituting monounsaturated and polyunsaturated fatty acids for saturated fatty acids can help lower health risks. (emphasis supplied)

3. National Cholesterol Education Program Adult Treatment Panel III

Evidence-based guidelines from the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health (National Cholesterol Education Program, 2002) recommend that low SFA-containing vegetable oils be used in moderate amounts as a means to help manage the risk of CHD.

> Vegetable oils and fats high in unsaturated fat do not raise blood cholesterol, but they have a high caloric density. These include **canola oil**, corn oil, olive oil, safflower oil, soybean oil, and sunflower oil.
>
> Liquid vegetable oils high in unsaturated fatty acids (e.g., **canola**, corn, olive, rice bran, safflower, soybean, sunflower) are recommended in moderation. (emphasis supplied)

4. American Heart Association

Dietary Guidelines from the American Heart Association (Krauss *et.al.*, 2000) recommend diets containing UFAs as alternatives to low-fat, high-CHO diets for the management of CHD risk:

> In conjunction with an energy intake suitable for maintaining a normal body weight, a diet high in unsaturated fat and low in saturated fat can be a viable

> alternative to a diet that is very low in total fat, particularly in individuals with an atherogenic dyslipidemia characterized by low HDL cholesterol, elevated triglycerides, and small dense LDL. This dietary approach entails replacing saturated fat calories with unsaturated fat calories rather than carbohydrate calories. A diet high in unsaturated fat may provide up to 30% of calories from monounsaturated and polyunsaturated fat, 10% of calories from saturated fat, and, 300 mg/d of cholesterol. As noted above, there is now clear evidence that total and LDL cholesterol levels are reduced comparably by replacement of saturated fat with either unsaturated fat or carbohydrate during weight maintenance conditions. Moreover, a diet relatively high in unsaturated fat can prevent or attenuate the decrease in HDL cholesterol and the increase in triglycerides that can occur in some individuals' response to a high carbohydrate, lower-fat diet. These latter effects may confer additional cardioprotective effects beyond LDL cholesterol lowering. Implicit to recommending a high unsaturated fat diet is that a healthy body weight be achieved and maintained.

The American Heart Association also acknowledges the potential cardioprotective effect of canola oil as a dietary source of ALA.

> There is some evidence from epidemiological studies that another n-3 fatty acid, α-linolenic acid, reduces risk of myocardial infarction and fatal ischemic heart disease in women... Because of the beneficial effects of n-3 fatty acids on risk of coronary artery disease as well as other diseases such as inflammatory and autoimmune diseases, the current intake, which is generally low, should be increased. Food sources of n-3 fatty acids include fish, especially fatty fish such as salmon, as well as plant sources such as flaxseed and flaxseed oil, **canola oil**, soybean oil, and nuts. (emphasis supplied)

5. Other organizations

Other professional organizations that recommend diets low in SFAs and cholesterol and high in UFAs but do not mention canola oil *per se* include the IOM (2002) and numerous international organizations such as the World Health Organization (2003), Health and Welfare Canada (1990), British Nutrition Foundation (1999), United Kingdom's Committee on Medical Aspects of Food and Nutrition Policy (1994) and Health Council of the Netherlands (2001).

In summary, a wide range of authoritative governmental and health professional organizations have acknowledged the cardioprotective properties of UFA-containing diets that are low in SFAs and cholesterol. Many of these organizations have identified canola oil as an important source of UFAs in their dietary recommendations, providing strong, credible support for the proposed claim.

E. Summary and conclusions

The information presented in this section clearly demonstrates that the weight of the available, credible scientific evidence supports the proposed "B" level qualified claim:

> Canola oil (19 grams – about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content, according to supportive but not conclusive research. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories.

This conclusion is supported by the totality of credible, scientific evidence and the precedent established by FDA's assessment of previous health claims, including the QHC for olive oil.

There is clear consensus among governmental and professional organizations that UFAs can reduce the risk of CHD when consumed as part of an energy-appropriate, moderate-fat diet that is low in SFAs and cholesterol. UFAs (MUFAs and PUFAs) have been shown to lower serum T-C and LDL-C in healthy human subjects by replacing dietary SFAs and probably by an independent mechanism unrelated to SFA intake. Therefore, UFAs are appropriate substances for the proposed claim.

Canola oil is lowest in SFAs and the most concentrated source of UFAs of all vegetable oils commonly consumed in the U.S. In addition, it contains substantial amounts of ALA, which

prospective observational studies and a clinical trial suggest reduces the risk of CHD in humans. Non-glyceride constituents of canola oil, including phytosterols and tocopherols, may also contribute to its cardioprotective effect.

All but three of the 21 intervention studies that met the minimum standards for review in this document provide strong or suggestive evidence that UFAs from canola oil have a favorable effect on serum lipids when fed as a replacement for SFAs. Significantly, nine of these studies are "persuasive" compared to only four persuasive studies supporting the olive oil claim. In addition, three of the five available studies found that canola oil lowered serum T-C and/or LDL-C concentrations significantly more than olive oil. Truswell and Choudhury (1998) suggested that this observation may be due to the higher SFA and lower PUFA content of olive oil compared to canola oil as well as its lower phytosterol content.

The U.S. Canola Association does not contest the validity of the olive oil QHC. However, the authorization of that claim provides a new basis of comparison for the assessment of claims pertaining to other sources of UFAs. Specifically, studies that compare a new UFA source to olive oil are now germane. In addition, the criteria used to evaluate the olive oil claim, including the characteristics and number of "persuasive" studies considered, provide additional benchmarks. The U.S. Canola Association, therefore, strongly believes that the available credible scientific evidence supports a "B" level QHC for canola oil in view of these new benchmarks.

F. Other scientific summary considerations

Additional scientific considerations for health claims specified in 21 C.F.R. § 101.70 (f) pertain mainly to their potential effect(s) on dietary intake. As noted previously, an extensive modeling study using data from the 1999-2002 NHANES was conducted to project the changes that would result from the substitution of canola oil for other vegetable oils in the U.S. diet. The effect of substituting canola oil-containing margarine for butter and margarines made with other fat sources was also determined. The study included 8,983 adults (≥20 years of age) for whom reliable 24-hour recall dietary data were available. The effect of substituting canola oil for other vegetable oils used directly, in cooking and in processed foods on energy and lipid intake was calculated. Three levels of substitution of canola oil (25%, 50% and 100%) were used to replace soybean, corn, cottonseed, safflower, sunflower and vegetable oils "not further specified"[15]. Canola oil was not substituted for olive, sesame or peanut oils because these oils tend to be used deliberately at the table or as an ingredient in recipes. Canola oil-based margarine (composed of 73% canola oil) was substituted for all butter and other margarines. The energy and lipid content of this margarine is presented in Table 4. A detailed report of the study is provided in Appendix B. This study is used, in part, to answer the questions addressed in this section of the petition.

1. Is there an optimum level of UFAs to be consumed beyond which no benefit would be expected?

The U.S. Canola Association believes the optimum level of UFAs as part of the proposed claim is 17.7 g/d – the minimum amount necessary to elicit a significant reduction in serum T-C and LDL-C concentrations (see section IV, page 74). The association is not aware of information that

[15] This term is used in the NHANES database to specify vegetable oil when the source was unknown.

Table 4
Energy and Lipid Content of Canola Oil-Based Margarine Used to Replace Butter and Margarine

Constituent	Content per 100 g
Energy (kcal)	700
Total fat (g)	79
Total SFAs (g)	10
Total MUFAs (g)	45
Total PUFAs (g)	22
Linoleic acid (g)	15
ALA (g)	7
Cholesterol (mg)	0

establishes a level beyond which dietary UFAs would no longer have a beneficial effect on serum lipids, however, intakes should not exceed the AMDRs for total fat (20 to 35% en), n-6 PUFAs (5 to 10% en) or ALA (0.6 to 1.2% en) established by the IOM (2002).

2. Is there any level at which an adverse effect from UFAs or foods containing UFAs (e.g., canola oil) occurs for any segment of the population?

As noted previously, canola oil has a beneficial fatty acid distribution and there are no known adverse effects associated with consumption of this oil. The current mean daily intake of canola oil among U.S. adults ≥20 years of age who participated in the 1999-2002 NHANES is presented in Table 5. These data show that the current intake of canola oil ranges from 0.9 g/d for men and women ≥70 years of age to 1.6 g/d for men 20-39 years of age. The average intake of canola oil for the entire population is 1.3 g/d or 0.55% en. The intake of canola oil expressed as percent of energy does not exceed 0.64% for any age/gender segment of the adult population. These values are substantially below the IOM's AMDR for total fat. Although analogous data are unavailable for children, it is reasonable to assume that intakes of canola oil are lower than those of adults due

to lower energy intake by this segment of the population. The AMDR for total fat for children (30 to 40% en) is higher than that for adults, which strongly suggests that the current intake of canola oil is free of any adverse effect on this population.

Table 5
Mean Intake of Canola Oil Among U.S. Adults

Gender and Age	Canola oil intake (g/d)	Energy intake (kcal/d)	Canola oil intake (% of energy)
Adults 20+	1.3	2196	0.55
20 - 29	1.3	2456	0.49
30 - 39	1.5	2415	0.56
40 - 49	1.4	2278	0.54
50 - 59	1.4	2112	0.61
60 - 69	1.2	1891	0.59
70+	0.9	1631	0.50
Men 20+	1.5	2592	0.51
20 - 29	1.6	2866	0.50
30 - 39	1.6	2834	0.52
40 - 49	1.4	2705	0.46
50 - 59	1.7	2469	0.61
60 - 69	1.3	2189	0.55
70+	1.0	1908	0.45
Women 20+	1.2	1831	0.58
20 - 29	1.1	2049	0.47
30 - 39	1.4	2015	0.62
40 - 49	1.3	1868	0.64
50 - 59	1.2	1765	0.61
60 - 69	1.1	1629	0.63
70+	0.9	1445	0.55

The projected intake of canola oil by U.S. adults, were it to replace 25%, 50% and 100% of the vegetable oils, butter and margarines noted above is presented in Table 6. The maximum mean percent of energy contributed by canola oil under this scenario is 14.4% among women ≥70 years of age. The mean percent energy from canola oil for the total population would be 12.4% en.

These values are substantially lower than the AMDR for total fat and demonstrate that maximum substitution of canola oil for other vegetable oils in the diet would not result in inappropriate levels of consumption.

Table 6
Projected Intake of Canola Oil Among U.S. Adults When Substituted for Select Vegetable Oils, Butter and Margarine

Gender and Age	25% replacement (% of energy)	50% replacement (% of energy)	100% replacement (% of energy)
Adults 20+	3.5	6.5	12.4
20 - 29	3.2	6.0	11.4
30 - 39	3.5	6.4	12.3
40 - 49	3.5	6.4	12.2
50 - 59	3.7	6.7	12.8
60 - 69	3.8	7.1	13.6
70+	3.8	7.0	13.5
Men 20+	3.3	6.1	11.8
20 - 29	3.1	5.7	11.0
30 - 39	3.3	6.2	11.8
40 - 49	3.2	6.0	11.5
50 - 59	3.5	6.4	12.1
60 - 69	3.7	6.9	13.2
70+	3.5	6.5	12.6
Women 20+	3.7	6.9	13.2
20 - 29	3.4	6.2	12.0
30 - 39	3.7	6.8	12.9
40 - 49	3.8	7.0	13.3
50 - 59	3.9	7.2	13.7
60 - 69	4.0	7.4	14.1
70+	4.0	7.5	14.4

In addition, as with the olive oil claim, the intent of the proposed claim is to encourage consumers to substitute a "healthier" oil for other forms of vegetable oil rather than to increase total intake. This intent is reflected in proposed language of the claim which states, "Canola oil should replace a similar amount of saturated fat in the diet without increasing calories." The data presented in

Table 7 show that replacement of other fat sources by canola oil and canola oil-based margarine does not appreciably change the intake of total fat.

Table 7
Projected Intake of Total Fat Among U.S. Adults When Canola Oil is Substituted for Select Vegetable Oils, Butter and Margarine

Gender and Age	0% replacement (% of energy)	25% replacement (% of energy)	50% replacement (% of energy)	100% replacement (% of energy)
Adults 20+	82.3	82.4	82.5	82.7
20 - 29	86.2	86.2	86.3	86.4
30 - 39	89.9	89.9	90.0	90.1
40 - 49	87.8	87.8	88.0	88.1
50 - 59	81.7	81.7	82.0	82.2
60 - 69	73.7	73.7	74.0	74.3
70+	61.2	61.2	61.6	61.9
Men 20+	96.9	97.0	97.1	97.3
20 - 29	99.5	99.5	99.5	99.6
30 - 39	105.3	105.3	105.4	105.5
40 - 49	104.2	104.3	104.4	104.5
50 - 59	95.5	95.6	95.7	95.8
60 - 69	85.3	85.5	85.6	86.0
70+	72.1	72.3	72.4	72.8
Women 20+	68.9	69.0	69.1	69.3
20 - 29	73.0	73.0	73.1	73.2
30 - 39	75.2	75.2	75.3	75.4
40 - 49	72.2	72.2	72.3	72.4
50 - 59	68.4	68.5	68.7	69.0
60 - 69	63.5	63.6	63.8	64.1
70+	53.9	54.1	54.3	54.7

The data presented above show that substitution of canola oil for other forms of vegetable oil, butter and margarine would not lead to excessive intakes with respect to the AMDR or alter the amount of total fat in the diet. Analogous data for two other IOM benchmarks, the AMDRs for PUFAs and ALA, are presented in Tables 8 and 9.

Table 8
Projected Intake of PUFAs Among U.S. Adults When Canola Oil is Substituted for Select Vegetable Oils, Butter and Margarine

Gender and Age	0% replacement (% of energy)	25% replacement (% of energy)	50% replacement (% of energy)	100% replacement (% of energy)
Adults 20+	6.8	6.3	5.7	4.6
20 - 29	6.2	5.6	5.1	3.9
30 - 39	6.7	6.1	5.5	4.4
40 - 49	6.9	6.3	5.7	4.6
50 - 59	7.2	6.6	6.0	4.8
60 - 69	7.3	6.7	6.2	5.1
70+	7.2	6.7	6.2	5.2
Men 20+	6.6	6.1	5.5	4.4
20 - 29	6.0	5.5	4.9	3.7
30 - 39	6.5	6.0	5.4	4.3
40 - 49	6.7	6.1	5.6	4.5
50 - 59	7.0	6.4	5.8	4.7
60 - 69	7.2	6.7	6.1	5.0
70+	6.9	6.4	6.0	5.1
Women 20+	7.0	6.5	5.9	4.7
20 - 29	6.4	5.8	5.2	4.0
30 - 39	6.9	6.3	5.7	4.5
40 - 49	7.1	6.5	5.9	4.7
50 - 59	7.3	6.7	6.2	5.0
60 - 69	7.4	6.8	6.3	5.2
70+	7.4	6.9	6.3	5.3

The mean projected intake of PUFAs under the three substitution scenarios described above fall below the upper range of the AMDR (10% en) for all age/gender segments of the population. One hundred percent substitution of canola oil and canola oil-based margarine is projected to yield PUFA intakes below the lower range of the AMDR (5% en) for some age/gender segments, however, it is very unlikely that the claim would have such an extreme effect on dietary intake among free-living individuals.

Table 9
Projected Intake of ALA Among U.S. Adults When Canola Oil is Substituted for Select Vegetable Oils, Butter and Margarine

Gender and Age	0% replacement (% of energy)	25% replacement (% of energy)	50% replacement (% of energy)	100% replacement (% of energy)
Adults 20+	0.8	0.7	0.8	1.1
20 - 29	0.6	0.7	0.8	1.0
30 - 39	0.6	0.7	0.8	1.0
40 - 49	0.6	0.7	0.8	1.1
50 - 59	0.7	0.8	0.9	1.1
60 - 69	0.7	0.8	0.9	1.2
70+	0.7	0.8	0.9	1.2
Men 20+	0.6	0.7	0.8	1.0
20 - 29	0.5	0.6	0.7	0.9
30 - 39	0.6	0.7	0.8	1.0
40 - 49	0.6	0.7	0.8	1.0
50 - 59	0.6	0.8	0.9	1.1
60 - 69	0.7	0.8	0.9	1.2
70+	0.6	0.8	0.9	1.1
Women 20+	0.9	0.8	0.9	1.1
20 - 29	0.6	0.7	0.8	1.0
30 - 39	0.6	0.7	0.9	1.1
40 - 49	0.7	0.8	0.9	1.2
50 - 59	0.7	0.8	1.0	1.2
60 - 69	0.7	0.8	1.0	1.2
70+	0.7	0.9	1.0	1.3

The mean projected intakes of ALA under the three substitution scenarios described above fall within the AMDR (0.6 to 1.2% en) for virtually all of the age/gender segments of the adult population. These intakes tend to be at the lower end of the range for the current diet (0% replacement) and at the higher end of the range for higher levels of canola oil substitution.

In summary, analysis of the 1999-2002 NHANES data shows that substitution of canola oil and canola oil-based margarine for vegetables oils, butter and other margarines would result in intakes

of total fat, PUFAs and ALA that are within the AMDRs. These data demonstrate that dietary changes induced by the proposed claim are very unlikely to have an adverse effect.

3. Are there certain populations that must receive special consideration?

As noted previously, dietary fats are ubiquitous components of the food supply, and recommended intakes are 30 to 40% en for 1- to 3-year old children and 20 to 35% en for adults. The replacement of higher SFA-containing fats with low SFA-containing fats (e.g., canola oil) is recommended for all individuals aged two and above by the Dietary Guidelines for Americans (U.S. Department of Health and Human Services, U.S. Department of Agriculture, 2005). Health claims do not apply to individuals less than two years of age, nor is canola oil a significant component of the diet of this population. In conclusion, the U.S. Canola Association is unaware of any populations that must receive special consideration as a result of the proposed claim.

4. What other nutritional or health factors (both positive and negative) are important to consider when consuming UFAs?

All dietary fats are a source of energy and have the potential to contribute to overfeeding and obesity if consumed in excess. However, this issue is not a concern because all fats have virtually the same caloric density and this proposed claim directs that canola oil be used as a substitute for other sources of fat. Therefore, the energy intake of individuals who adhere to the proposed claim will not change. FDA acknowledged this fact in allowing use of the olive oil claim.

On the other hand, as noted previously, increased use of canola oil, at the expense of other fats, would have a favorable effect on dietary lipids due to its desirable fatty acid distribution. The

effect of replacing 50% and 100% of vegetables oils, butter and margarine with canola oil and canola oil-based margarine, as described above, on various dietary lipid components is presented in Table 10.

Table 10
Projected Change in Dietary Lipid Parameters Among U.S. Adults When Canola Oil is Substituted for Select Vegetable Oils, Butter and Margarine

Lipid Parameter	50% replacement		100% replacement	
	Absolute change	Percent change	Absolute change	Percent change
SFAs (g/d)	-1.1	-4.2	-2.3	-8.7
SFAs (% en)	-0.5	-4.7	-1.0	-9.4
SFAs (% of subjects with <7% en)	3.2	18.9	8.1	47.9
SFAs (% of subjects with <10% en)	5.8	12.6	11.6	25.3
MUFAs (g/d)	4.2	13.7	8.4	27.4
MUFAs (% en)	1.7	13.8	3.4	27.6
PUFAs (g/d)	-2.8	-16.8	-5.5	-32.9
PUFAs (% en)	-1.1	-16.1	-2.2	-32.4
PUFAs (% of subjects with <10% en)	7.4	8.6	11.6	13.6
ALA (g/d)	0.6	40.0	1.1	73.3
ALA (% of subjects meeting the AI)	19.4	41.9	30.8	65.5
Cholesterol (mg/d)	-1.4	-0.50	-2.8	-1.0

These data show that canola oil substitution would have favorable effects on the intake of SFAs,

MUFAs, PUFAs and ALA and a minimal effect on dietary cholesterol. A 50% substitution of canola oil for soybean, corn, cottonseed, safflower, sunflower and "vegetable oils not further specified" would result in a decrease of 1.1 g SFAs per day (a 4.2% reduction) among the adult U.S. population. The effect of a 100% substitution would result in a decrease of 2.3 g/d (9.4% reduction). In addition, the percentage of subjects who would meet the current Dietary Guidelines for Americans recommendation of <10% en SFAs (U.S. Department of Health and Human Services, U.S. Department of Agriculture, 2005) would increase by 12.6% and 25.3% for a 50% and 100% replacement, respectively. Analogous data for the NHLBI recommendation of <7% en dietary SFAs for CHD patients (National Cholesterol Education Program, 2001) are an increase of 18.9% and 47.9% for a 50% and 100% replacement, respectively.

There are no minimum recommendations for MUFA consumption, but the intake of these fatty acids would increase by 4.2 g/d (a 13.7% increase) and 8.4 g/d (27.4% increase) for a 50% and 100% replacement, respectively. As noted in the studies supporting the olive oil claim, MUFAs may help reduce the risk of CHD when substituted for unhealthy fats in the diet.

Total PUFA intake, namely n-6, would decrease substantially with the substitution of canola oil for other fat sources. This substitution would result in a decrease of dietary PUFAs by 16.8% and 32.9% for a 50% and 100% replacement, respectively. The number of individuals who would meet the NHLBI recommendations to consume <10% en of these fatty acids (National Cholesterol Education Program, 2002) would increase by 8.6% and 13.6% for the lower and higher replacement rates, respectively.

ALA (n-3) intake would increase substantially with the substitution of canola oil for other fat sources. A 50% substitution rate would increase ALA intake by 0.6 g/d (a 40% increase), while a 100% substitution rate would raise dietary ALA by 1.1 g/d (a 73% increase). The number of individuals who meet the AI for ALA of 1.1 g/d for women and 1.6 g/d for men would increase by 42% and 66% for a 50% and 100% substitution rate, respectively.

Dietary cholesterol would change only minimally upon canola oil substitution because the mean daily contribution of this dietary constituent from butter (the only cholesterol-containing food affected by the substitution) is relatively small.

In conclusion, analysis of the 1999-2002 NHANES data shows that substitution of canola oil and canola oil-containing margarine for most other vegetable oils, butter and margarine does not increase energy or total fat intake, but has beneficial effects on the intake of SFAs, MUFAs, PUFAs and ALA *vis à vis* recommendations from the Dietary Guidelines for Americans, NHLBI and the IOM.

G. Prevalence of CHD in the U.S. population and relevance of the claim in the context of the total daily diet

As noted previously, CHD is the leading cause of death in the U.S. and accounted for 53% of all mortality due to cardiovascular disease in 2002 (American Heart Association, 2005). The magnitude of CHD as a public health priority is reflected in the fact that FDA has authorized several CHD-related health claims since enactment of the Nutrition Labeling and Education Act, including dietary saturated fat and cholesterol and risk of coronary heart disease (21 C.F.R.

§ 101.75); fruits, vegetables, and grain products that contain fiber, particularly soluble fiber, and risk of coronary heart disease (21 C.F.R. § 101.77); soluble fiber from certain foods and risk of coronary heart disease (21 C.F.R. § 101.81); soy protein and risk of coronary heart disease (21 C.F.R. § 101.82); and an interim final rule for plant sterol/stanol esters and risk of coronary heart disease (21 C.F.R. § 101.83). Furthermore, FDA has allowed the use of three CHD-related QHCs for conventional foods: nuts and CHD[16], walnuts and CHD[17] and MUFAs from olive oil and CHD[18].

The proposed claim clearly places the potential benefits of UFAs from canola oil within the context of the total daily diet. As noted previously, the proposed language of the claim states that UFAs from canola oil "…should replace a similar amount of saturated fat in the diet without increasing calories."

The U.S. Canola Association believes that these observations demonstrate that CHD is a prevalent condition in the U.S. and that the claim provides valuable information in the context of, and is relevant to, the total daily diet.

H. UFAs are a substance under 21 C.F.R. § 101.14 (a)(2)

The definition of a "substance" under 21 C.F.R. § 101.14 (a)(2) is "…a specific food or component of food, regardless of whether the food is in conventional food form or a dietary supplement that includes vitamins, minerals, herbs, or other similar nutritional substances." UFAs (including oleic acid, linoleic acid and ALA) are components of food that provide energy to the body and are key

[16] http://www.cfsan.fda.gov/~dms/qhcnuts2.html.
[17] http://www.cfsan.fda.gov/~dms/qhcnuts3.html.
[18] http://www.cfsan.fda.gov/~dms/qhc-sum.html#olive.

components in membrane structural lipids – especially nervous tissue myelin (IOM, 2002). Linoleic acid and ALA are essential fatty acids and AIs have been established for them by the IOM (2002). Finally, FDA concluded that MUFAs from olive oil meet the definition of substance in the health claim regulation because they are a "component of food". The U.S. Canola Association believes the same reasoning applies to the proposed claim and concludes that UFAs from canola oil meet the definition of "substance" under 21 C.F.R. § 101.14 (a)(2).

IV. MINIMUM EFFECTIVE DOSE

The U.S. Canola Association calculates 19 grams of canola oil per day as the minimum effective dose for the proposed claim. The amount of UFAs from canola oil that must be consumed each day to provide the potential beneficial effect on CHD was calculated using the same general approach FDA used to determine this value for the olive oil claim. For the olive oil claim, the agency calculated the difference in the amount of MUFAs (% en) between the high-MUFA and high-SFA experimental diets in the applicable studies used to support the claim. These values were multiplied by 2,000 kcal (the daily energy intake used for nutrition labeling) and converted to grams (i.e., 1 g MUFA = 9 kcal). FDA determined that, "…the lowest amount of MUFAs needed to replace SFAs that may result in significant reduction in serum total and LDL-C is 17.5 g of MUFAs." This value corresponds to 23 g olive oil (i.e., 74% of the fatty acids in olive oil are MUFAs).

Table 11 presents information from the nine most persuasive studies that compared canola oil diets with diets higher in SFAs.

Table 11
Difference Between UFA Intake and Serum Lipids in the Nine "Persuasive" Studies Comparing Diets Rich in Canola Oil and SFAs

Reference	**ΔUFAs (%en)**	**ΔUFAs (g/2,000 kcal)**	**ΔT-C (%)**	**ΔLDL-C (%)**
Baudet and Jacotot (1988)	9.5	21.2	-17.0	-21.0
Karvonen *et.al.* (2002)	3.3	7.3	-5.1	-6.6
Kratz *et.al.* (2002)	11.5	25.5	-14.3	-17.5
Matheson *et.al.* (1996)	2.1	4.7	-7.0	-10.0
Noakes and Clifton (1998)	7.6	16.9	-8.4	-12.8
Seppanen-Laakso *et.al.* (1992)	5.4	12.0	-3.0	-6.4
Uusitupa *et.al.* (1994)	13.4	29.7	-21.6	-29.5
Valsta *et.al.* (1992)	9.1	20.2	-15.5	-24.0
Wardlaw *et.al.* (1991)	10.0	22.2	-8.8	-11.8
AVERAGE	8.0	**17.7**	-11.2	-15.5

As noted earlier, all of the most persuasive studies found that canola oil-containing diets prompted favorable changes in serum lipids. Specifically, T-C fell by 3.0% to 21.6% and the range of decrease for LDL-C was 6.4% to 29.5%. Casual inspection of these data show, as would be expected, that there is a dose-response relationship between the change in UFA intake and the resulting decrease in serum T-C and LDL-C.

In the case of olive oil, FDA used the most responsive study to establish a value of 17.5 g MUFAs per day as the minimum effective "dose" for that claim. Using this approach, a value of 4.7 g UFAs per day would be established for canola oil because Matheson *et.al.* (1996) showed that this change in UFA intake resulted in a significant[19] drop in both T-C and LDL-C. However, the U.S. Canola Association believes a more conservative approach is appropriate, using the average difference in UFAs from all of the most persuasive studies (17.7 g UFAs per day) as the minimum effective daily dose (see Table 11 above). This value is equivalent to 19 grams of canola oil based on its UFA content of 92.9%.

The use of 19 grams of canola oil as a minimum effective dose for the proposed claim is consistent with current dietary patterns for American adults observed in the 1999-2002 NHANES. The data presented in Table 12 show the percent of substitution of canola oil and canola oil-based margarine that would be required to achieve the minimum effective dose for each age/gender segment of the U.S. population.

[19] FDA has established an informal policy that a decrease of 4% to 5% in T-C and LDL-C is significant with respect to health claims.

Table 12
Percent Substitution of Canola Oil and Canola Oil-Based Margarine Necessary to Achieve the Minimal Effective Daily Dose of 19 g per Day

Gender and Age	Intake of Fats Targeted for Replacement (g/d)	Percent Substitution of Canola Oil Required to Provide the Minimum Daily Dose (19g/d)
Adults 20+	28.9	65.7
20 - 29	29.8	63.7
30 - 39	31.4	60.5
40 - 49	29.6	64.1
50 - 59	28.6	66.5
60 - 69	27.3	69.5
70+	23.6	80.5
Men 20+	32.4	58.8
20 - 29	33.4	56.8
30 - 39	35.5	53.5
40 - 49	33.1	57.4
50 - 59	31.5	60.3
60 - 69	30.7	62.0
70+	25.7	73.8
Women 20+	25.7	72.3
20 - 29	26.3	72.3
30 - 39	27.5	69.2
40 - 49	26.3	72.2
50 - 59	25.8	73.8
60 - 69	24.4	77.7
70+	22.2	85.7

These data demonstrate that the percent substitution of canola oil for other fat sources necessary to achieve the minimum effective daily dose ranges from 59% for men to 72% for women. The U.S. Canola Association believes that this magnitude of substitution is achievable through the regular use of canola oil and canola oil-based margarine.

V. NATURE OF THE FOOD ELIGIBLE TO BEAR THE CLAIM

The U.S. Canola Association recommends that products that contain at least 4.75 grams of canola oil per RACC and are low in saturated fat (21 C.F.R. § 101.62(c)(2)), contain no more than one gram of *trans* fatty acids per RACC, and contain no more than 20 mg cholesterol per RACC be eligible to bear the proposed claim. Canola oil and canola oil-containing products would be exempted from the total fat disqualifier level, and canola products that are predominantly canola oil (i.e., spreads, shortenings, salad dressings) would be exempted from the 10% DV nutrient contribution requirement. All of the other general health claim requirements in 21 C.F.R. § 101.14 would apply.

A. Minimum amount of canola oil per RACC

As noted above, 19 grams of canola oil per day is sufficient to lower T-C and LDL-C by at least four percent when consumed as part of a diet low in saturated fat. The U.S. Canola Association proposes that a minimum of 4.75 g canola oil per RACC be required for a food to bear the claim. This amount is based on the premise that consumers should have the flexibility to consume the minimum effective dose by eating up to four servings of canola oil-containing foods per day (19.0 g ÷ 4 servings/d = 4.75 g/serving).

FDA has traditionally considered that a typical daily food consumption pattern is composed of three meals and a snack per day (58 *Federal Register* 2302, 2379, January 6, 1993). This dietary pattern was used to define the minimum content criterion for three CHD-related health claims: soy protein (64 *Federal Register* 57700 at 57713); ß-glucan soluble fiber from whole oats (62 *Federal*

Register 3584 at 3592); and soluble fiber from psyllium seed husks (63 *Federal Register* 8103, 8109, February 18, 1998).

FDA also used this approach to establish 6 g olive oil per RACC as the minimum amount required for products to be eligible for that claim. The agency stated:

> To determine the minimum amount of olive oil necessary to be in a food, the agency considered the number of eating occasions at which consumers might consume olive oil or olive oil products and the number of potential foods that could be labeled with a qualified health claim about MUFAs from olive oil and CHD. Foods in these categories can be part of every eating occasion, and the typical American eating pattern is three meals and one snack per day. Therefore, the determination of the qualifying level of MUFAs form olive oil for a food to bear the claim will be based on four eating occasions per day.

The U.S. Canola Association fully agrees with this approach and believes that it applies equally to canola oil. Many consumers may choose to incorporate canola oil into their diets throughout the day by using the essentially pure product in cooking, as a salad dressing or other direct use. However, the availability of a wide variety of canola oil-containing products would provide additional opportunities for consumers to obtain the benefit of this high-UFA food. For example, margarines are commercially available that contain between 5.3 and 5.8 g canola oil per 10 gram serving[20]. Use of the proposed claim on such products has the potential to call attention to their availability in the marketplace and to provide consumers with additional options to manage CHD risk by using them as substitutes for higher SFA-containing foods such as butter.

Furthermore, one of Congress' original objectives for the Nutrition Labeling and Education Act was to provide incentives for food manufacturers to develop products that help consumers eat

[20] http://www.canolaharvest.com/usa/products/CH_margarine/index.html .

healthier diets. The establishment of a reasonable criterion for the minimum amount of canola oil necessary for foods to be eligible to bear the claim will provide food manufacturers with such incentives. In addition, the availability of such a criterion will increase the ability of food manufacturers to minimize the total fat content of products that qualify for the claim. Finally, it is important to maintain consistency in the approach used to determine this criterion with the olive oil claim. A lack of consistency in this area would be confusing to consumers and unfair to the canola industry. In conclusion, the U.S. Canola Association strongly recommends that a value of 4.75 g canola oil per RACC be established as a minimum criterion for foods eligible to bear the proposed claim.

B. Total fat content

The majority of currently authorized CHD-related health claims (21 C.F.R. §§ 101.75, 101.77, 101.81) require that foods meet the "low-fat" definition (21 C.F.R. §101.62 (b)(2)) in order to be eligible to bear a claim. However, the U.S. Canola Association does not believe such a criterion is appropriate for the proposed claim.

Leading public health authorities have altered traditional recommendations that Americans consume a low-fat, high-carbohydrate diet as a means to reduce the risk of CHD because it is now recognized that restricting the intake of SFAs and TFAs is more important than limiting total fat. For example, the fifth edition of the Dietary Guidelines for Americans (U.S. Department of Agriculture, U.S. Department of Health and Human Services, 2000) modified the previous "fat" guideline from, "choose a diet low in fat, saturated fat, and cholesterol" to "choose a diet that is low in saturated fat and cholesterol and **moderate in total fat"** (emphasis supplied). This

principle was extended to the 2005 Dietary Guidelines, which recommend that up to 35% of energy be provided by fats that are high in UFAs (U.S. Department of Health and Human Services, U.S. Department of Agriculture, 2005). Similarly, the IOM (2002) established an AMDR for total fat of 20 to 35% of energy for the same reason. Finally, the Nutrition Subcommittee of FDA's Food Advisory Committee voted unanimously (with two abstentions) on April 28, 2004[21] that the answer to the question, "Does the current scientific evidence suggest a relationship between total fat intake and risk of coronary heart disease?" is "no."

FDA has recognized in its consideration of health claims and QHCs that the low-fat criterion is not always appropriate for CHD-related health claims. For example, the agency initially proposed that foods eligible to make the soy-CHD claim be required to be low in fat, but eliminated this requirement because total fat intake is not directly related to CHD and because the inherent fat content of soybeans would have prevented many products made from whole beans from making the claim (64 *Federal Register* 57700 at 57717). The agency also chose not to impose a low-fat criterion on products eligible to make the sterol/stanol ester health claim because fat is the only vehicle capable of delivering these cardioprotective substances which were deemed to have public health significance (65 *Federal Register* 54686 at 54708). FDA also noted that this policy was consistent with the fifth edition of the Dietary Guidelines for Americans, which recommends "moderate" rather than "low" fat diets. More recently, the agency allowed a qualified health claim for nut-containing products that are low in saturated fat and cholesterol, but not necessarily low in total fat[22]. Finally, FDA has extended this position to the QHC for olive oil[23]:

[21] http://www.fda.gov/ohrms/dockets/ac/04/minutes/4035m1_FinalSummaryMinutes.htm .
[22] http://www.cfsan.fda.gov/~dms/qhcnuts2.html .
[23] http://www.cfsan.fda.gov/~dms/qhcolive.html .

> …FDA concurs with current dietary guidelines that consuming diets low in saturated fat and cholesterol is more important in reducing CHD risk than consuming diets low in total fat. Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion, that olive oil, vegetable oil spreads, dressings for salads, shortenings, and olive oil-containing foods that bear a MUFAs from olive oil and CHD qualified health claim meet the "low fat" criterion.

In summary, the U.S. Canola Association believes there is now compelling evidence that foods need not be low in total fat in order to reduce the risk of CHD as long as they are low in saturated fat, *trans* fat and cholesterol. FDA has acknowledged this fact in previous rulemakings and QHC petitions. Therefore, it is requested that a low-fat criterion not be imposed on foods eligible to bear the proposed claim.

C. Saturated and *trans* fat content

The U.S. Canola Association believes that all canola oil-containing products eligible to bear the proposed claim should be required to be low in saturated fat as specified in 21 C.F.R. § 101.62(c)(2). As noted previously, canola oil has the lowest SFA content of all commonly consumed edible oils in the U.S. and this food inherently meets the low-saturated fat definition. Similarly, such products should contain no more than one gram of TFAs per RACC as described in the agency's final rule (68 *Federal Register* 41434, July 11, 2003). If FDA establishes a nutrient content claim for low TFAs in the future, it should be added to the criteria for the proposed claim. This criterion would help ensure that consumers who choose products bearing the proposed claim reduce SFA and TFA intake as they transition to higher UFA-containing foods.[24] Canola oil, which meets the current FDA labeling definition for zero TFAs, would clearly meet any potential criterion set for low TFAs with respect to the proposed claim.

[24] FDA declined to set a disqualifying level for TFAs in the olive oil QHC.

D. Cholesterol content

All of the CHD-related health claims that have been authorized to date require that eligible foods be low in cholesterol as defined by 21 C.F.R. § 101.62 (d). Like all plant-based foods, canola oil does not contain cholesterol. The U.S. Canola Association believes that canola oil-containing formulated products should be required to contain ≤ 20 mg cholesterol per RACC (or per 50 g if the RACC is 30 g or less or two tablespoons or less) according to 21 C.F.R. § 101.62(d)(2)(ii)(A) in order to be eligible to bear the proposed claim.

E. Exemptions

As noted above, canola oil and canola oil-containing products would need to be exempted from the total fat disqualifier level, 21 C.F.R. § 101.14(e)(3), in order to qualify for the proposed claim. In addition, canola oil and products that are predominantly canola oil (e.g., shortenings, salad dressings) would need to be exempted from the 10% DV nutrient contribution requirement, 21 C.F.R. § 101.14(e)(6). FDA accommodated similar exemptions for olive oil-containing products and the U.S. Canola Association believes a similar accommodation is equally justifiable for products containing canola oil.

1. Total fat disqualifier level

As noted in paragraph "B" above, nutrition science and public health policy have evolved to recognize the benefits of moderate-fat diets that are low in SFAs, TFAs and cholesterol as alternatives to more traditionally advocated low-fat, high-carbohydrate diets. In addition, analysis of the totality of credible scientific evidence presented in this document clearly demonstrates that UFAs from canola oil have beneficial effects on CHD risk factors when consumed as part of a

moderate-fat diet that is low in SFAs, TFAs and cholesterol. Despite their health benefits, products that are essentially pure canola oil, and many canola oil-containing products that would otherwise be eligible to bear the proposed claim, would fail to meet the total fat disqualifier level as defined in 21 C.F.R. § 101.14(a)(4). Therefore, the U.S. Canola Association respectfully requests an exemption from these requirements.

FDA has established an important precedent for granting exemptions from the total fat disqualifier level when appropriate to do so. Such an exemption was granted for products making the sterol/stanol ester health claim. The agency cited four criteria it considered in making this decision (65 *Federal Register* 54686 at 54709), including whether the disease in question was of public health significance; whether the absence of an exemption from the disqualifier level would severely limit the number of foods that would qualify to bear the claim; whether there was evidence that the population to which the health claim was targeted was not at risk for the disease; and whether there were other public health reasons for granting the exemption.

FDA concluded that sterol/stanol ester-containing foods should be granted the requested exemption because CHD is a significant public health concern, lack of an exemption would severely limit the foods that would qualify for the claim and sterol/stanol ester-containing products have a significant potential to benefit public health by virtue of the fact that they can lower serum T-C and LDL-C without adversely affecting HDL-C. The agency also justified the exemption by concluding that "…current scientific evidence does not indicate that diets high in unsaturated fat are associated with CHD…" and cited the 2000 Dietary Guidelines for Americans, which states,

"Choose a diet that is low in saturated fat and cholesterol and **moderate in total fat**" (emphasis supplied).

More recently, FDA allowed the use of a QHC for whole or chopped nuts that exceed the total fat disqualifier level. The agency concluded that "…an appropriately qualified claim about consumption of most nuts would assist consumers in maintaining healthy dietary practices, provided that the label bears a disclosure statement that compiles with 21 C.F.R. § 101.13(h) (i.e., 'see nutrition information for fat content.')[25]."

Finally, the agency decided to exempt olive oil and olive oil-containing products from the total fat disqualifier level. In making this decision FDA noted:

> The most and least persuasive scientific studies that suggested a relationship between MUFAs from olive oil in replacement of SFAs and reduced risk of CHD used olive oil incorporated into several types of foods that are traditionally high in fat, namely vegetable oil spreads, dressings for salads, and shortenings… Foods that contain these levels of fat will necessarily exceed the disqualifying total fat level. If FDA imposed the disqualifying total fat level on these products, it would prevent these products, which were included in the scientific studies that suggested a relationship, from bearing the claim. Olive oil-containing foods are generally not vehicles for delivering fat. However, given that FDA intends to exercise enforcement discretion for olive oil products that contain 6 g or more olive oil per RACC, the food may be formulated with additional olive oil and still contribute to the claimed effect, FDA concludes that applying the disqualifying levels of total fat to olive oil-containing foods would unduly limit the foods that could contribute to beneficial effects from bearing the claim.

The U.S. Canola Association believes that all of the criteria used by FDA to justify the total fat disqualifier level exemption for sterol/stanol ester-containing foods, whole or chopped nuts and

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[25] Letter to Mr. D.J. Soetaert from Dr. Christine L. Taylor dated July 14, 2003 (Docket No. 02P-0505) http://www.cfsan.fda.gov/~dms/qhcnuts2.html .

olive oil-containing foods also apply to the proposed claim for UFAs from canola oil. Specifically, CHD is a disease of major public health significance; failure to grant an exemption would prevent pure canola oil and many other canola oil-containing foods from making the claim and canola oil and canola oil-containing foods have the potential to substantially reduce the risk of CHD among U.S. consumers. The U.S. Canola Association, therefore, respectfully requests that the exemption be granted. Food products exempted from this provision would be required to bear a disclosure statement that complies with 21 C.F.R. § 101.13(h).

2. 10% DV Minimum Nutrient Content Requirement

Foods must contain at least 10% DV of protein, dietary fiber, calcium, iron, vitamin A or vitamin C per RACC in order to bear a health claim unless otherwise exempt by regulation (21 C.F.R. § 101.14 (e)(6)). The agency explained the rationale for this requirement in the preamble to its final rule on the general principles concerning approval of health claims (58 *Federal Register* 2478, 2521, January 6, 1993) which states, "Thus, FDA finds merit in the suggestion that foods bearing health claims should be those consistent with dietary guidelines, and that the value of health claims should not be trivialized or compromised by their use on foods of little or no nutritional value."

Since the initial rulemaking for health claims, FDA has proposed to exempt certain fruits and vegetables as well as many enriched grain products from the 10% DV nutrient contribution requirement (60 *Federal Register* 66206, 66214, December 21, 1995). The agency's proposal states, "…diets high in fruits, vegetables and grain products have been associated with various specific health benefits, including lower occurrence of coronary heart disease… and therefore, are exactly the types of foods that should be included in the diet to reduce the risk of specific diet-

related diseases." FDA further stated that it would consider providing additional exemptions from the 10% DV requirement if it were provided with sound justification to do so.

Indeed, the agency granted such a request for salad dressings to bear the sterol/stanol ester claim (65 *Federal Register* 54686 at 54711) and for walnuts to bear the QHC for reduced risk of CHD. Finally, FDA exempted olive oil-containing salad dressings and shortenings from this provision for the olive oil claim:

> Olive oil, certain vegetable oil spreads, dressings for salads, and shortenings do not meet the 10% minimum nutrient content requirement of 21 C.F.R. 101.14(e)(6). However, olive oil, certain vegetable oil spreads, dressings for salads and shortenings provide MUFAs that can be used in place of SFAs in the diet. FDA believes that information to help consumers reduce saturated fat and cholesterol consumption would assist consumers in maintaining healthy dietary practices. If FDA did impose the 10% minimum nutrient content requirement for these food categories, it would prevent these major olive oil products, which were included in the scientific studies that suggested a relationship, from bearing the claim. Therefore, FDA has decided not to consider, in the exercise of its enforcement discretion, that olive oil, dressings for salads, and shortenings that bear a MUFAs from olive oil and CHD qualified health claim meet the 10% minimum nutrient content requirement.

The U.S. Canola Association believes that all of the criteria used by FDA to justify exemption from the 10% DV minimum nutrient content requirement for sterol/stanol ester-containing foods, whole or chopped nuts and olive oil-containing foods also apply to the proposed claim for UFAs from canola oil. The association, therefore, respectfully requests that an exemption to this provision be granted for canola oil as well as for vegetable spreads, dressings for salads and shortenings made predominantly from canola oil.

VI. LABELING REQUIREMENTS

Foods eligible to bear the proposed claim would be required to declare the grams of MUFAs and PUFAs per serving in the Nutrition Facts panel as stipulated in 21 C.F.R. § 101.9(c)(2)(iii)-(iv).

VII. ANALYTICAL METHODS (DETERMINATION OF COMPLIANCE)

There are no Association of Analytical Chemists (AOAC) approved methods that would allow FDA to determine the canola oil content of products that bear the proposed claim. However, in cases where the claim appears on products that are essentially pure canola oil, compliance will be obvious because the RACC for such products is 30 g, and the weight of any non-canola oil ingredients are insignificant. For products that are composed primarily of non-canola oil ingredients, compliance with the claim will not be obvious.

The U.S. Canola Association proposes that information supplied by the manufacturer be used to establish compliance when the claim is used on formulated foods that are not essentially pure canola oil. This approach is similar to that used to determine the eligibility of products to bear the health claim for soy protein and CHD (21 C.F.R. § 101.82 (c)(2)(ii)(B)). This provision requires manufacturers to maintain records such as "… recipes or formulations, purchase orders for ingredients…" or any other information that reasonably substantiates the claim. In addition, the U.S. Canola Association proposes that manufacturers choosing to make the claim be required to maintain records sufficient to substantiate the claim for as long as the products are marketed, and to provide these records upon written request to FDA.

VIII. PROPOSED MODEL HEALTH CLAIMS

Possible model wording for the proposed claim was studied using consumer research with wording from the current olive oil claim as a benchmark[26]. The U.S. Canola Association believes that alternative claim language, which scores at parity or higher with respect to "clarity" compared to the olive oil claim and conveys the same level of scientific uncertainty, should be allowed.

A. Consumer research: Composition of the panel and methodology

A demographically and geographically balanced sample of 1,012 U.S. consumers 21 to 64 years of age was used to rate the clarity, believability and level of scientific uncertainty of the current olive oil claim modified to reflect a "B" level claim for canola oil and four alternative claims. The research was conducted over the Internet between August 30 and September 6, 2005 using the consumer panel from Greenfield Online®. The characteristics of the sample, which was patterned after the U.S. Census, are presented in Table 12.

The Greenfield Online® panel is composed of more than 5.7 million individuals and closely reflects the demographic makeup of the U.S. population with respect to gender, age, geographic location, education level, income, ethnicity and occupation. Detailed information on this panel is provided in Appendix C. A much larger sample size can be used with online research compared to mall-intercept studies, which enhances the ability to obtain samples that are representative of the total U.S. population.

[26] The object of the claim was changed to canola oil and the word "limited" was removed for the purposes of this research to provide a valid comparison with the "B" level claims proposed for canola oil in this petition.

Table 12
Demographic Characteristics of 1,012 Consumer Research Participants

Characteristic	Percent of subjects
Age	
▪ 21-34	33
▪ 35-54	51
▪ 55-64	17
Region	
▪ Northeast	19
▪ Midwest	23
▪ South	36
▪ West	22
Ethnicity	
▪ White/Caucasian	81
▪ Black/African American	11
▪ Hispanic	9
▪ Asian or Pacific Islander	3
▪ Mixed Racial Background	3
▪ Some other Race	3

The exact wording of the benchmark claim (designated as "FDA Generic") and four alternative claims (identified by key qualifying words) for canola oil used in this research were:

FDA Generic
Eating about 1½ tablespoons (19 grams) of canola oil daily may reduce the risk of coronary heart disease due to the unsaturated fat in canola oil. FDA evaluated the data and determined that, although there is research supporting the claim, the evidence is not conclusive. To achieve this possible benefit, canola oil should replace a similar amount of saturated fat and not increase the total number of calories you eat in a day.

Uncertainty Remains
Canola oil (19 grams - about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories. FDA has determined that although some scientific uncertainty remains, the weight of the evidence supports this conclusion.

Data Are Limited
Canola oil (19 grams - about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories. FDA has concluded that while the scientific data are limited, the majority of available evidence supports this statement.

Suggests, But Does Not Prove
Canola oil (19 grams - about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content, according to scientific evidence that suggests, but does not prove, this benefit. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories.

Supportive, But Not Conclusive
Canola oil (19 grams - about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content, according to supportive but not conclusive research. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories.

Consumers were first asked to provide demographic and geographic information and agreed to a question regarding survey confidentiality. Approximately 200 consumers (range 201-205) were then shown one of the test claims. The sample was selected to ensure that the consumer demographics were similar for each claim. The subjects were asked to rate the claim on a five-point scale for measures of clarity, believability and scientific uncertainty. The data obtained from this section of the survey are referred to as "monadic scores" because each participant saw only one claim. Subjects were then shown the FDA generic claim or one of the alternative claims (selected at random) if they had already seen this claim and asked to choose which statement was more clear and easier to understand as well as which claim was more believable. Next, the consumers were shown a list of the qualifying language for each of the five test claims and asked to rate scientific uncertainty according to "…how sure you think the authors of the statement are that canola oil helps reduce the risk of heart disease." The data obtained in this section are referred

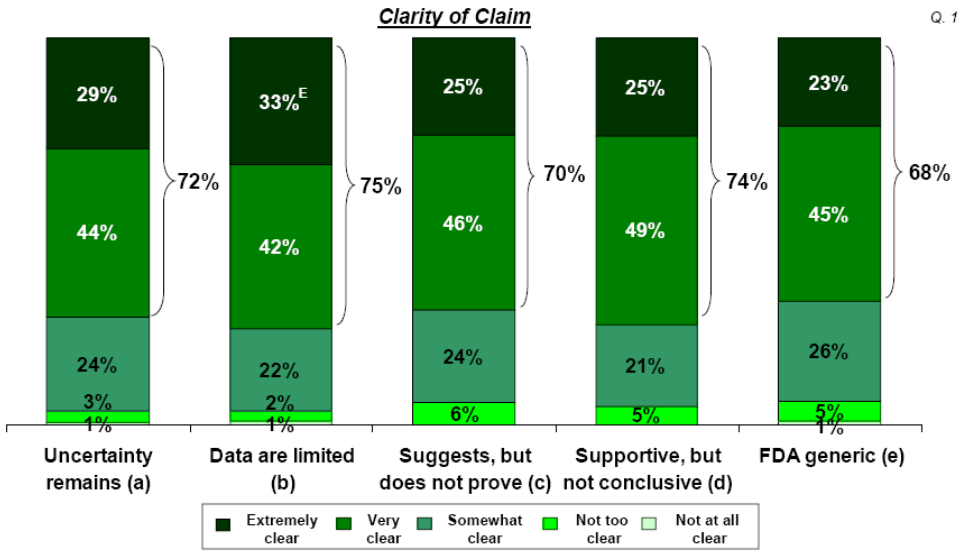
to as "comparative monadic scores." The final section of the survey pertained to perceptual data on canola oil and is not germane to the proposed claim.

B. Consumer research results

Complete results of the portions of the research that are germane to the proposed claim are provided in Appendix D. As noted above, the U.S. Canola Association believes that claims at parity with the FDA generic claim for clarity/ease of understanding and level of scientific uncertainty should be allowed for the proposed claim.

The monadic scores presented in Figure 2 show that all five of the test claims were similar ($p>0.05$) with respect to clarity. Between 68% and 75% of respondents rated the five claims as either "extremely" or "very" clear. These data show that any of the five claims are capable of being understood by the majority of consumers.

Figure 2
Monadic Ratings for Clarity of Test Health Claim Language



The monadic scores presented in Figure 3 show that "supportive, but not conclusive" and "suggests, but does not prove" were closest to the FDA generic claim with respect to the level of scientific uncertainty. All three claims were similar ($p>0.05$) in the percentage of consumers who stated the author was "completely sure" and "very sure" that canola oil helps reduce the risk of CHD. However, when these two ratings were combined, "suggests but does not prove" had a slightly (but statistically significant, $p<0.05$) higher rating (lower level of scientific uncertainty) in this category than the other two claims. However, the three claims were virtually identical in ratings of scientific uncertainty, according to the comparative monadic scores shown in Figure 4. The comparative scores were more sensitive than pure monadic scores because the consumers had an opportunity to compare all five claims. Consequently, these data provide compelling evidence that "suggestive, but inconclusive" and suggests, but does not prove" are at parity with the FDA generic claim with respect to level of scientific uncertainty.

Figure 3
Monadic Ratings for Scientific Certainty of Test Health Claim Language

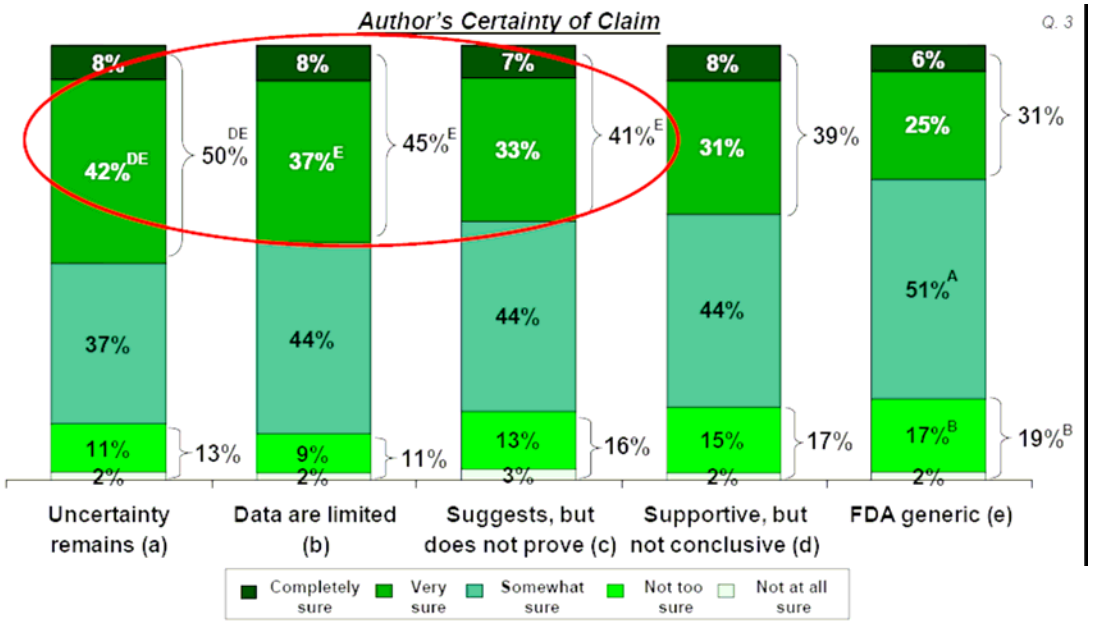
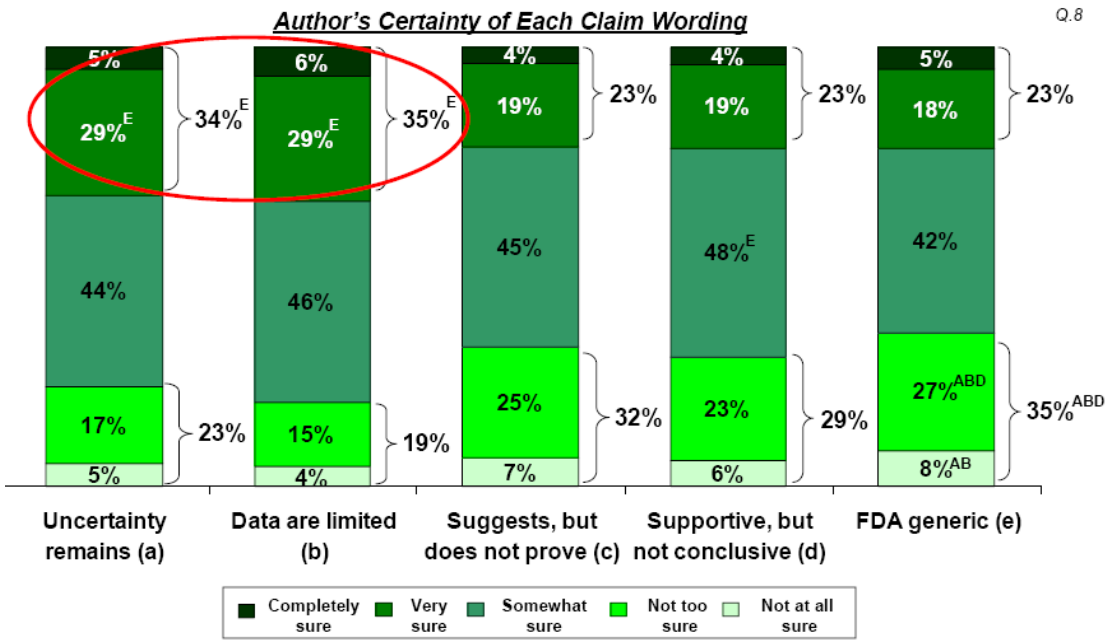


Figure 4
Comparative Monadic Ratings for Scientific Certainty of Test Health Claim Language



C. Recommended health claim language

Based on the consumer research summarized above, the U.S. Canola Association recommends that FDA exercise its enforcement discretion with respect to the following two QHCs:

> Canola oil (19 grams - about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content, according to supportive but not conclusive research. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories. One serving of this product contains X grams canola oil.

> Canola oil (19 grams - about 1½ tablespoons per day) may reduce the risk of coronary heart disease due to its unsaturated fat content, according to scientific evidence that suggests, but does not prove this benefit. Canola oil should replace a similar amount of saturated fat in the diet without increasing calories. One serving of this product contains X grams canola oil.

The appropriate disclaimer statement "[see nutrition information for total fat content]" will also be provided immediately adjacent to the claim with no intervening material as specified in 21 C.F.R. § 101.13(h).

In conclusion, the U.S. Canola Association believes that FDA should exercise its enforcement discretion for the two health claims specified above. These claims are supported by consumer research that shows they are equivalent to the olive oil claim with respect to clarity and level of scientific uncertainty. Furthermore, the agency decided to allow wording similar to "suggests, but does not prove" for the QHC for nuts and CHD after considering consumer research similar to that summarized above and has permitted wording similar to "suggestive but inconclusive" for the QHC for walnuts and CHD. In addition, FDA approved the phrase "according to supportive but not conclusive research" in a QHC for EPA and DHA as dietary supplements.[27]

IX. ENVIRONMENTAL IMPACT ASSESSMENT

The U.S. Canola Association chooses to avail itself of the categorical exclusion with respect to an environmental impact assessment provided by 21 C.F.R. § 25.32(p). Accordingly, an environmental impact assessment is not required for this submission.

[27] http://www.cfsan.fda.gov/~dms/qhc-sum.html#omega3

X. CONCLUSION AND CERTIFICATION

In conclusion, the U.S. Canola Association strongly believes that the totality of credible scientific evidence supports the proposed "B" level QHC for UFAs from canola oil and reduced risk of CHD. There is ample evidence to demonstrate that UFAs from canola oil have favorable effects on serum lipids when consumed by healthy adults as part of a diet low in SFAs. In addition, there is ample scientific evidence to show that canola oil is as good as or better than olive oil in this regard. Moreover, canola oil contains non-glyceride components that may contribute to its cardioprotective effects. Substitution of canola oil for other vegetable oils would help consumers meet recommendations in the 2005 Dietary Guidelines for Americans by reducing the intake of SFAs and would also favorably affect dietary MUFAs, PUFAs and ALA. Availability of the proposed claim will promote public health by helping educate consumers about this simple, affordable strategy to reduce the risk of CHD and may encourage manufacturers to substitute canola oil for other oils with less favorable fatty acid profiles. The U.S. Canola Association, therefore, respectfully requests that FDA allow use of the proposed claim as quickly as possible.

I hereby certify that, to the best of my knowledge, this petition is a representative and balanced submission that includes unfavorable information as well as favorable information known to me to be pertinent to the evaluation of the proposed qualified health claim.

Respectfully submitted,

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